THE CANADIAN MEDICAL ASSOCIATION

LE JOURNAL DE

L'ASSOCIATION MÉDICALE CANADIENNE

JULY 22, 1961 • VOL. 85, NO. 4

MEN AND BOOKS

TO CULTIVATE THE GROVES OF ACADEMUS*

WILDER PENFIELD, M.D., D.Sc., F.R.S., F.R.C.S.(Eng.), F.R.C.P.(Eng.), F.R.C.S.[C], *Montreal*

TODAY, in the City of Athens, if you pass along the highway that leads out toward the laurel grove where Greeks celebrate the national wine festival, you will come to a block in the traffic. An ancient olive tree stands in a little patch of earth in the centre of the street, and crowding men and donkeys turn aside to pass it, like a rushing stream around a stone. Trucks halt and truckers honk impatiently. If it is spring and the festival is on, the crowding is worse and resentful faces peer out at the tree from sleek limousines on their way to the tasting of the wine.

The gigantic trunk is no more than a hollow shell, but lusty daughters are growing from its roots and grey-green olive leaves ripple along their branches, fresh and new like the leaves of the parent tree when it was young, 2300 years ago. This, Athenians say, is the sole survivor of the olive trees in the famous Grove of Academus. This tree stood outside the walls of Athens on the banks of a now-vanished stream called Cephissus. Here it was that Plato walked with his disciples and talked of abstract ideas, morals and mathematics.

That talk still echoes in the academic halls of our colleges today. Our students wear the cap and gown derived no doubt from the elegant cap and the short cloak which Plato's pupils wore. This, the uniform of higher learning, was even then the target of jests from the townsmen. Only the phrase, "egg head", was left to the inspiration of a "nitwit" in the twentieth century.

I would like to look at the grove of Academus and then consider the problem of how to cultivate the academic groves around the world today. But first, a word about Plato: This was a nickname, as everyone knows, given to the aristocratic young Athenian. He was called by his parents Aristocles, but was commonly known as Platon, from the word *platos* meaning broad. This doubtless described his neck and shoulders, for he had been a wrestler in the Isthmian games. These were famous Panhellenic athletic competitions held in Corinth. They were second only to the Olympic games, in the eyes of the citizens of greater Hellas.

This broad-shouldered young man was handsome, popular and versatile. He was said to delight in Euripides, athletics and the admiration of women. When he reached the age of 20 he was apparently hesitating between a career in poetry and one in politics. But he abandoned all such ideas when Socrates, that strange ugly philosopher, came his way and he fell under the Socratic spell.

Socrates was a teacher who had no academy, no place to teach. Instead, he walked to and fro in the agora of Athens, enquiring into the minds of men, probing their motives, seeking to define the good, to discover a soul, to put into words some concept of ethical behaviour. The material for his study was to be found in men's minds. He searched for a spirit beyond the mind and a spirit beyond the gods of Mount Olympus. He seemed to perceive the presence of a being behind the gods of Greece who was not so different from the conception of the Christian God in the minds of men today.

When Plato met Socrates, he burned his own poems and joined the followers of this new master. He went about with him, making notes of his conversations, until that dramatic day when the citizens of Athens could stand the recurring sting of the "gadfly" no longer, and Socrates was called upon to drink the poison hemlock.

That was in the year 399 B.C. when the disciple Plato was probably 28 years of age. He saw that his carefree, confident youth was at an end, and he left Athens in despair and anger. Thirteen years followed during which he wandered about, to live in many cities and to study in the mathematical school of the Pythagoreans. He served as a soldier, too, and finally he was captured and sold into

*The York Lecture, University of British Columbia, October 29, 1960, inaugurating the new Department of the History of Medicine and Science under the chairmanship of Dr. William C. Gibson.

slavery. His friends in Athens heard of it and ransomed him. So he came back home at the age of 41.

On his arrival there, the man who had paid for his ransom, Anniceris by name, refused to accept from Plato's other friends the sums that they had raised. Consequently three thousand drachmas were left over. They converted that into the first recorded academic endowment! It was invested in the olive grove, on the banks of the Cephissus, which was called the Grove of Academus. This became, then, Plato's home and when pupils came to him from the city it was soon converted to an institution of higher learning. In time, it was called *Academia* according to Plutarch, who quoted a contemporary description as follows: "A beautiful, well-watered garden where philosophers meet and express their irreligious views on the nature of the gods." Obviously *Academia* had its adverse critics, but it also had its ardent supporters since it continued as an intellectual centre for nine centuries.

In Plato's lifetime there were numerous gifts and endowments directed to the teacher, since Plato, unlike other philosophers throughout Greece, charged no fee to his disciples. Suidas stated that "from time to time [rich men] bequeathed in their wills, to members of the school, the means of living a life of philosophic leisure." Obviously these served as continuing fellowships. Diogenes Laertius states that the tyrant Dionysius II was reported to have given Plato the unbelievable sum of eighty talents, about $480,000. "This," Will Durant has pointed out dryly, "might explain the philosopher's patience with the King."

There is no record of what the admission requirements to *Academia* may have been, but at least we know that there was an inscription over the entrance that read: *medeis ageometretos eisito* —which might be translated, "Let no one enter here without geometry."[1]

I have asked you to look back with me across the whole history of academic institutions to the first one: back to the Grove of Academus. What was going on in that grove was also going on elsewhere in ancient Greece, and had been for a century and more. Here a poet, there an astronomer or a mathematician, musician, sculptor, painter, philosopher, orator, historian or tragedian emerged from the ranks of educated citizens. Soon disciples came to him to listen and learn and to strike out for themselves, or to turn to other teachers.

It was the random blossoming of genius as though in a garden whose fateful seeding had been kept a secret from those whose task it was to tend it. The soil, in which such varied genius germinated, was Greek education. That system of education was common throughout greater Greece, made up of many City-States, some ruled by tyrants but more of them by democratic election. In spite of the independence of so many states, the Greeks were truly one people using a common literature and a common religion and folk lore. Greek religion differed from all others in this: There was no prohibition against new thinking. The gods, like the Greeks themselves, seemed to consider freedom essential and natural.

For a long time, strange to say, the only formal bond of union between these independent cities was the Panhellenic league of sports. From the days when they first appeared in history while conquering and settling the shores of the eastern Mediterranean, on down to the culmination of their civilization, they took delight in athletic games conducted always before the temple of a Greek god.

Athletic festivals soon came to include contests of the mind as well as of the body. Greek contestants, naturally, sought to outstrip their opponents, but there was an aim beyond that for which we have no word today. It consisted in the production of a supreme performance, carried out perhaps in an agony of effort. They called this *aretê*. It has been translated "virtue" in the writings of Plato. Virtue, however, has in it an element of goodness that is not included in *aretê*, and it lacks the sense of effort and agony which *aretê* includes. *Aretê*, Greeks believed, was what pleased the god before whom the games were held. It brought admiration from other Greeks. Kitto[2] has described this essential national ideal as "outstanding excellence . . ." "It was *aretê*," he said, "that the games were designed to test—the *aretê* of the whole man, not merely a specialized skill." This outstanding excellence was what the Greek student, teacher, artist and thinker was expected to set up for himself as his own personal aim.

In recent years the surprising fact has become apparent to the great nations that intellectual leadership is the goal, the prize above all else, to be sought in world-wide competition. Defence, and perhaps survival, may depend on superiority of the mind, and not on the circumference of a biceps as in times gone by.

Today, governments are turning, bewildered and perhaps not quite convinced, to their own academic institutions, expecting much. But excellence does not come on command, nor genius either. Little added speed can be forced from a long-starved horse by shouts or the use of a whip.

Those of us who watch today from the Groves of Academus see a world in rapid change. New nations struggling to their feet look about for guidance. Men who have little of this world's goods are demanding more, in what Dean Rusk[3] has aptly called the "revolution of rising expectations". Across the world we see the mounting tides of population that will bring the nations to a famine unless the birth rate is reduced.

We watch the giants struggle for their ideologies in which the brotherhood of man has been forgotten—communist dictatorships striving to expand, capitalist freedoms in confused opposition. We see

the gathering clouds of fear and suspicion and hear the rumbling thunder of atomic threats.

Ministers of Defence may turn to the universities demanding more physicists and more chemists. But what the people of the world want, and need, is leadership of mind and spirit. They want to find the path toward kindness and the brotherhood of man and peace. And where can it be found if not in the institutions that have sought the truth since the days of Socrates and Plato? The cure for our problems is probably not to be discovered by physicist or chemist. But no one can predict in what soil genius will flower, nor can the nature of that flowering be predetermined.

Here is our problem: How can we, in Canada, bring forth genius as the Greeks did? If it will not come to command, can it be bought? The answer to this, it seems to me, is "yes", but only if accompanied by certain changes in society.

Most scholars will agree that the intellectual contribution of Greece in classical times was unique. Such a thing has only happened once in the whole history of mankind. How could the Greeks, who were neither numerous nor wealthy, achieve so much? Was the Greek type an evolutionary variant? Did he have better muscles, stronger bones and a superior brain?

I believe the answer to that must be "no". Since history began, there has been no definite evidence of further structural improvement in the brain of man. The Greeks did not discover writing for themselves, or how to sail a ship. When they migrated down from an unknown region of northern Europe to Crete and the coasts of the eastern Mediterranean, they were taught these things and much else by the people they conquered. Their alphabet came from the Phoenicians, and doubtless their seamanship. The kindred people that they left behind were not outstanding, nor are their own descendants living on in Greece today. The secret of Greek genius must be found in the conditions of Greek life between the sixth and third centuries B.C. It must lie in the background of Greek education as it developed in the cities of the Ægean.

During the dark ages the Greeks had been forgotten. Then the medieval universities came into being when Greek and Latin scholarship was rediscovered in a great renaissance of learning. In North America, colleges and universities sprouted here and there in pioneer days. They taught the learning of the past but they did not reach a position of leadership.

Then about 100 years ago a merchant in Baltimore created a Board of Trustees for a hospital and a university. He did so without supplying one adjective to describe how these boards should use the prospective endowment. When he died, the largest educational bequest in history, up to that time, came to the Johns Hopkins University.

Mr. Hopkins was a Quaker, an unassuming bachelor of simple tastes. He is reported to have talked with Fowler, his English gardener, one day as follows:

"This estate, Fowler, is to be the site of a great university, a place where the young men of coming generations will have the opportunity which I have always longed for. Young men will study great things here under these trees that thee and I have planted, and yonder, over nearer to the Patapsco, will be a great hospital. I have thought it all out, Fowler. All my family shall be taken care of according to their needs but after that is done, all I own shall go to these two children of mine, a university and a hospital.

"Like the man in the parable, I have had many talents given to me and I feel they are in trust; I shall not bury them but give them to the lads who long for a wide education and who will do great things someday with the knowledge they receive here in this university . . .They shall have a chance right here under the shadow of these old trees."[4]

So Mr. Johns Hopkins gave funds and freedom to a well-selected board. The members of the board in turn called for advice from Eliot of Harvard University, Angell of Yale and White of Michigan. They suggested nothing new. Daniel Coit Gilman was called to be the President of the new university. Funds and complete freedom were given to that young man. And something akin to inspiration, that Eliot and Angell and White had failed to propose, came to him:

He built a university geared to graduate teaching. And, to this end, he seemed to have the gift of "second sight" in the selection of men both young and old. His university contained creators, new professors who were previously unrecognized as leaders, men like William Osler and his colleagues in the medical school, Gildersleeve in classics and many others. The Johns Hopkins became the first university in the western world capable of competing in creative scholarship with the universities of Europe.

Following the Hopkins example, graduate teaching and research improved, and American and Canadian universities came of age in the eyes of the world. Some degree of genuine leadership came to us then, and the initiating impetus for this advance in university work at the graduate level was derived from an endowment gift by a Quaker merchant who also gave freedom for local development.

During the first and second decades of the twentieth century a new phenomenon appeared in the United States. John D. Rockefeller, like Johns Hopkins, decided not to bury the golden talents that had come to him. He created, instead, a remarkable group of Foundations. His declared purpose was "to promote the well-being of mankind throughout the world". Vast sums of money were directed by the trustees to education and to hospitals. The largest single project was the building and development of the first good medical

school in China, a project on which the colossal sum of forty-two million dollars was eventually expended. It is a project not forgotten even now in China, for the Peking Union Medical School still leads in that country.

The spending by the Rockefeller Foundation all around the world was motivated solely by altruism and informed realism. No finer thing has emerged in our modern capitalist society. The Montreal Neurological Institute came into existence in 1934 with Rockefeller assistance. But the pattern followed was more important than the money given. The Foundation helped to create it, and left a nucleus of scientific endowment; then withdrew from the field, leaving the Institute to grow and live on local support. It has grown and will make its independent contribution in a future that has no foreseeable end.

Many other foundations have been created since then until there are, at present, more than 11,000 such goodly organizations in the United States alone. The giving of money by these foundations has provided a beneficial stimulus, of course. But there is no solution, in this sort of giving, for the support of academic work—far from it! Furthermore, objectionable features have developed with the vast increase in short-term grants for research. Heads of departments and even heads of universities are sometimes led into a scramble for these short-term grants. They have been known to cut their research projects to fit the whims of those who hand out charity for academic work. They are like bribes to induce scholars to work on "this" instead of "that". Sometimes professors even try to run a teaching department with the crumbs that fall from a research grant!

Governments have followed the lead of these foundations in a big way. But they have not copied the original Rockefeller Foundation scheme of starting some special work, setting a school or department or an institute on its feet, endowing it and then leaving it to fare as it can with continuing local support—no, not that. They have taken up the giving of short-term grants. That brings annual gratitude which has political advantages. So the Medical Research Council of Britain, the National Research Council in Ottawa, the National Science Foundation in Washington, and more recently the Canada Council have given remarkable temporary emergency assistance to science and a little to original work in the arts.

But direct federal support to universities has also appeared during this era of short-term grants. It has taken different forms in different countries:

Look at the Soviet Socialist Republic first. Support of academies, universities and research institutes is centralized and administered from a federal focus through a system of national academies. The money provided to the professor and to the institutions is often adequate and the support of student fellowships is excellent. This is the extreme example of support for ulterior purpose with little freedom. The over-all return will be disappointing.

There is in Russia little or no independence at the periphery. Research in fields that are not considered important by Moscow would not be supported. Political and philosophical and religious reasoning and writing, if truly independent and frank, would not be encouraged to say the least, and certainly would not be supported.

What is independence without the right to follow lines of thought which those in authority may consider to be a waste of time? What is freedom if one cannot voice opinions contrary to popular dogma? How can universities evolve better things for this world without both freedom and local independence?

In Britain now, with her socialist type of government, they stand somewhere between the Russian and the Canadian systems of support. While in England this summer I made exhaustive enquiry from this particular point of view. Even in the two ancient endowed universities of Oxford and Cambridge, costs have risen so that the local income from endowment is now very far short of adequate support. Many millions must be contributed annually from the central government to each university through the University Grants Committee.

These grants are used for routine expenses and for research and for building. It must be said at once that the University Grants Committee has always been composed of public-spirited, intelligent citizens. Grants are made for five years in advance. Nevertheless, the grants for support of academic re-organization or for teaching projects or research, for every university in the land, are dispensed or withheld by the same small group. Grants are refused according to the opinions and prejudices of that Committee.

I will not attempt contemporary description of education in Canada or the United States. Others could do it far better than I. My own conclusion is derived from historical perspective. It has been tested during my own lifetime as university student, teacher, departmental administrator and research worker. My conclusion is that higher education calls for simultaneous support and endowment grants from government.

First and last: The most certain guarantee of freedom and independence to any university is endowment. At least half of the financial support of any such institution should come from permanent income arising in invested funds. Grants from governments to universities and institutes should be accompanied by a simultaneous proportional endowment. For every hundred dollars that such an institution receives from government for annual expense and building there should be one hundred dollars of endowment.

At the end of twenty to twenty-five years, with bold investment, you may say, a university would be independent, like the private institutions of the

past. The answer to that must be, "no". Expansion, growth and rising costs will prevent the government from being discharged so easily of its responsibility.

That, you may complain, would mean doubling the immediate burden of the financing of higher education. Exactly! The intellectual excellence of the Greeks *can* be bought for Canada. But the price is high and the conditions are exacting.

My proposal, I know, would not be accepted by a totalitarian government, and for obvious reasons. It would not be accepted by any government that feared intellectual freedom and independence. In Canada, if even the Federal Government alone were to accept this basis of university assistance it would contribute enormously to the freedom and the independence of higher education throughout the land. It would do this, too, without interfering in the conduct of local universities.

Yes, Canada all alone could do what Greece did. The Canadian brain is just as good as the brain of any Athenian who came to walk with Plato in the Grove of Academus. Canada could give intellectual leadership to a world-in-danger, if she would cultivate her "academic groves".

The price of support—doubling the present costs—would be small indeed when seen in true perspective: money for simultaneous support and endowment, conditions which provide freedom and independence for academic institutions, athletics for all in the growing years, competition for those who are competitive, rewards and applause for excellence in every field of human endeavour and, with it all, freedom of expression.

Solon, the law-giver of Athens, counselled the Greeks to lead temperate lives. "Nothing in excess," he said, "all things in due proportion."

Let us train the body and use it, train the brain and turn the mind to the achievement of excellence. If our students and teachers had support and similar independence, with similar rewards, they would do what the classical Greeks did.

But before these things can come about, we must develop a national admiration for that peculiar quality the Greeks called *aretê*, admiration for outstanding excellence in any field of human endeavour.

REFERENCES

1. DURANT, W.: The Life of Greece, Simon & Shuster, Inc., New York, 1939.
2. KITTO, H. D. F.: The Greeks, Penguin Books Ltd., Harmondsworth, Middlesex, 1951.
3. RUSK, D.: The President's Review, Rockefeller Foundation Annual Report, New York.
4. FLEXNER, A.: Daniel Coit Gilman, creator of the American type of university, Harcourt, Brace and Company, New York, 1946.

Canad. M. A. J.
July 22, 1961, vol. 85

ORIGINAL ARTICLES

THE MACROCYTOSIS OF HEPATIC DISEASE: THIN, THICK AND TARGET MACROCYTOSIS*

J. R. BINGHAM, M.D., F.R.C.P.[C], *Toronto*

Two out of three patients with hepato-biliary disease have abnormally large erythrocytes. Although the presence of these large red cells, or macrocytes, was recognized in the blood of patients with liver disease as long ago as 1883,[1] there has been no agreement about their frequency, origin or significance. This paper reports the findings of a study of the macrocytes found in the blood of 222 patients suffering from a variety of hepatic and biliary tract diseases.

Three Types of Macrocytes

A macrocytic blood picture, or macrocytosis, is one in which the mean cell diameter of the erythrocytes is 7.60 microns (μ) or more by the method of measurement used in this study.† Sixty-two per cent of the 222 patients had a macrocytic blood picture.[2]

Early in the study it became apparent that there was not one macrocyte, but three different macrocytes, occurring singly or together in various proportions in the blood of these patients. These three types of macrocytes were termed thin, thick and target macrocytes. Macrocytosis can therefore be defined, according to the predominant macrocyte present, as thin macrocytosis, thick macrocytosis, or target macrocytosis.

Detailed observations on thin and thick macrocytosis have been published elsewhere.[2, 3] The present report contains a summary of those observations and new and unpublished observations on target macrocytosis.

Thin Macrocytosis

In thin macrocytosis all of the macrocytes are thin (Fig. 1). This was the commonest type of macrocytosis and was found in 81 patients or 59% of all the patients with macrocytosis (Table I). The thin macrocyte is a flattened erythrocyte, round in shape. Its diameter is greater than that of the normal erythrocyte, its thickness is less, but its volume is the same (compare Column A with Column B in Table II). As the flattening becomes greater, the cell diameter progressively increases and thickness decreases.[2] Its hemoglobin is distributed uniformly throughout the cell, and the biconcave shape of the normal erythrocyte is not seen.

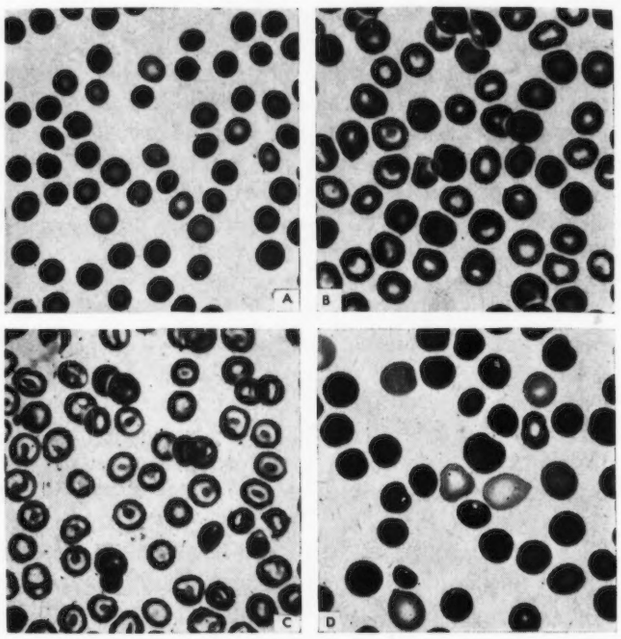


Fig. 1. — Normal erythrocytes and the three types of macrocytosis occurring in hepatic disease. (a) Normal erythrocytes. RBC (red blood cell) count 5,120,000; MCD (mean corpuscular diameter) 7.16 μ; anisocytosis 0.49 μ; MCV (mean corpuscular volume) 96 μ^3. Normoblastic marrow. (b) Thin macrocytosis. RBC count 4,650,000; MCD 8.86 μ; anisocytosis 0.69 μ; MCV 101 μ^3. Macronormoblastic marrow. (c) Target macrocytosis. RBC count 4,400,000; MCD 8.00 μ; anisocytosis 0.82 μ; MCV 101 μ^3. Macronormoblastic marrow. (d) Thick macrocytosis. RBC count 1,600,000; MCD 8.4 μ; anisocytosis 0.82 μ; MCV 131 μ^3. Megaloblastic marrow. Magnification 650 diameters.
This figure was reproduced from *Blood*[2] with permission of the publisher.

Blood and Bone Marrow Picture

Inspection of the blood films may show uniform enlargement of the erythrocytes or a striking degree of anisocytosis. When the cells are uniformly enlarged, the presence of macrocytosis may not be recognized without actual measurement of the cells. The leukocytes and platelets are normal. Anemia is usually not marked (Table II).

The bone marrow films of patients with thin macrocytosis usually show macronormoblastic maturation, but atypical megaloblastic maturation was seen in one case.

Origin of Thin Macrocytes

There are two theories of origin of thin macrocytosis, which may be called "central" and "peripheral" (Larsen).[5] These theories were based on studies in which the types of macrocytosis were not separated into the three types. However, from inspection of the reports it would appear that the macrocytosis was predominantly of the thin type. Those workers who supported the "central" theory

*From the Department of Medicine, Toronto Western Hospital and University of Toronto, Toronto.
This work was supported by a grant from the National Research Council of Canada. Reprint requests should be addressed to 399 Bathurst Street, Toronto.

†The mean cell diameter was measured by projecting specially stained blood films on to paper at 2000 magnification. The outlines of 200 unselected erythrocytes were traced on to the paper and their diameters measured. From this the mean cell diameter and the standard deviation of the mean cell diameter were calculated. The standard deviation was used as a measurement of anisocytosis.

TABLE I.—HEPATIC DISEASE AND THE THREE TYPES OF MACROCYTOSIS

	Total No. of patients	*No macrocytosis*	*Thin macrocytosis*	*Thick macrocytosis*	*Target macrocytosis*
Laennec's cirrhosis					
(a) Alcoholic	96	29	43	14	10
(b) Non-alcoholic	9	4	4	1	0
Infectious hepatitis	37	24	10	0	3
Subacute yellow atrophy	7	1	3	2 (1)	1*
Biliary cirrhosis	14	5	4	0 (3)	5†
Carcinoma of liver, pancreas, or gall bladder	38	10	9	0	19
Choledocholithiasis	10	6	4	0	0
Other benign obstruction	4	2	1	0	1
Miscellaneous‡	7	4	3	0	0
	222	85	81	17	39

*Target and thick types combined in 1 patient.
†Target and thick types combined in 3 patients.
‡Includes hepar lobatum, 2 patients; hemochromatosis, 2 patients; primary amyloidosis, polyserositis, undiagnosed granulomata, 1 patient each.

believed that the macrocytes arose from defective maturation in the bone marrow.[4, 5] Those workers who favoured the "peripheral" theory believed that the erythrocytes were normal when delivered from the bone marrow but that they underwent swelling[6, 7] or flattening[8, 9] in the peripheral circulation and thus became macrocytic. The results from the present study supported the central theory and may be summarized as follows:

1. If thin macrocytes arise through a flattening of normal erythrocytes in the peripheral circulation, all of the erythrocytes should be enlarged equally and anisocytosis would be unchanged. However, in our patients anisocytosis was found to vary greatly from patient to patient in a manner not compatible with any peripherally operating factor.

2. The maturing erythrocytes in the bone marrow of patients with thin macrocytosis were themselves macrocytic (macronormoblastic maturation).

3. Normal-sized donor erythrocytes were transfused into the circulation of four control subjects and four patients with thin macrocytosis. Samples were recovered and their diameters measured. The transfused normal-sized donor cells did not become macrocytic, which suggests that a mechanism capable of flattening normal erythrocytes was not present in the recipients' circulation.[2]

Clinical Findings

Studies were made[2] to determine whether thin macrocytosis was related to any of the following: (1) type of hepatic disease; (2) signs of hepatic disease; (3) abnormal liver function tests; (4) severity of hepatic disease.

(1) The percentage of patients with thin macrocytosis, according to type of hepato-biliary disease, is shown in Fig. 2. Thin macrocytosis occurred in all types of hepato-biliary diseases with about equal frequency, which suggests that the kind of hepato-biliary disease was not of major etiological importance. Further studies revealed that thin macrocytosis did not occur in patients suffering from simple fatty liver or uncomplicated obstruction of the common bile duct of short duration. In both of these conditions hepatic cell damage was absent. These observations suggested that thin macrocytosis is related to hepatic parenchymal cell damage as such, rather than to any specific type of hepatic parenchymal cell damage.

(2) The presence of thin macrocytosis was not related to the presence of jaundice, spider nevi, hepatomegaly or splenomegaly. However, a significant correlation was found between the presence of thin macrocytosis and the presence of ascites and/or edema. The significance of this correlation was not determined.

TABLE II.—ERYTHROCYTE MEASUREMENTS OF HEALTHY PEOPLE AND OF PATIENTS WITH HEPATO-BILIARY DISEASE AND THIN MACROCYTOSIS, THICK MACROCYTOSIS AND TARGET MACROCYTOSIS

	A	*B*	*C*	*D*
Mean cell diameter (μ)	7.14 (6.80 - 7.49)	7.94 (7.60 - 8.90)	8.17 (7.60 - 8.91)	7.91 (6.89 - 8.86)
Mean cell thickness (μ)	2.30 (1.90 - 2.60)	2.01 (1.6 - 2.3)	2.27 (2.0 - 2.7)	2.00 (1.70 - 2.40)
Anisocytosis (μ)	0.45 (0.34 - 0.56)	0.60 (0.40 - 1.07)	0.85 (0.55 - 1.25)	0.65 (0.35 - 1.55)
Mean cell volume (μ^3)	95 (86 - 100)	99 (73 - 110)	123 (110 - 160)	101 (81 - 115)
Mean cell hemoglobin concentration (%)	31 (28 - 34)	30 (22 - 36)	30 (22 - 37)	28 (20 - 115)
Erythrocyte count (millions per c.mm.)	4.80 (4.10 - 5.60)	3.62 (1.60 - 5.40)	2.67 (1.27 - 4.40)	3.58 (2.15 - 4.70)

A. Normal erythrocytes—22 healthy people. B. Thin macrocytosis—81 patients with liver disease. C. Thick macrocytosis—17 patients with liver disease. D. Target macrocytosis—39 patients and 8 other patients with 10% or more target cells but whose erythrocytes had a mean cell diameter below 7.60 μ.

Canad. M. A. J.
July 22, 1961, vol. 85

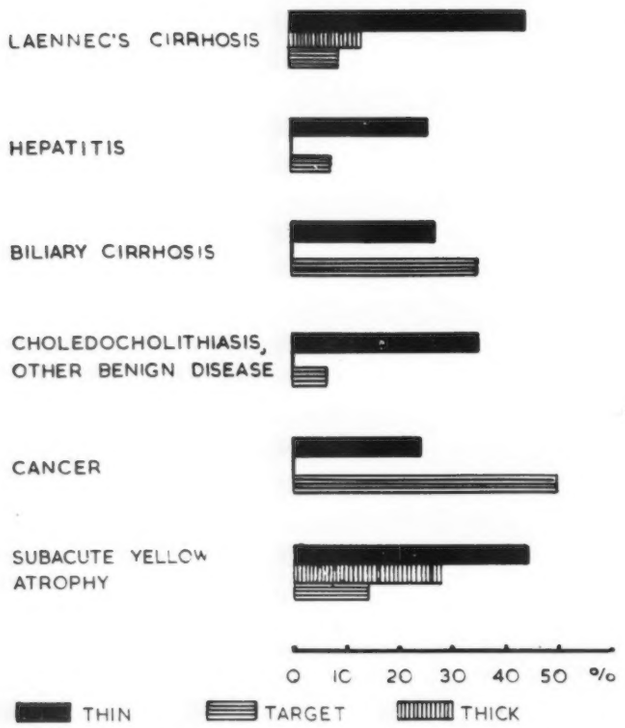


Fig. 2.—The % frequency of thin, target and thick types of macrocytosis in the various types of hepatic disease. This figure was produced from *Blood*[2] with permission of the publishers.

(3) The presence of thin macrocytosis was not related to abnormalities of the following tests of liver function: van den Bergh, bromsulphalein retention, alkaline phosphatase, cholesterol, albumin, globulin, albumin-globulin ratio, or cephalin-cholesterol flocculation.

(4) Thin macrocytosis appeared as frequently among patients with non-fatal hepatic disease as among patients with fatal hepatic disease.

Relation to Diet, Folic Acid, Liver and Vitamin B_{12}

No correlation was found between the nutritional value of pre-hospital diets of patients with Laennec's cirrhosis and the presence or absence of thin macrocytosis. The parenteral administration of large doses of folic acid, liver and vitamin B_{12} had no effect on the blood and bone marrow abnormalities of patients with thin macrocytosis. Neither a deficiency of iron nor bleeding caused this disorder.[2]

The vitamin B_{12} content of livers obtained at autopsy from 14 patients with and without thin macrocytosis was estimated. No correlation was found between the vitamin B_{12} level and macrocytosis. Some patients without thin macrocytosis had very low vitamin B_{12} levels, whereas other patients with thin macrocytosis had normal vitamin B_{12} levels.[2]

In view of the foregoing and our inability to relate thin macrocytosis to anything but hepatic parenchymal cell disease (and ascites and/or edema), we concluded that thin macrocytosis reflected a particular response to non-specific hepatic parenchymal cell disease. For some unknown reason hepatic cell damage is followed by an alteration of erythrocyte maturation from normoblastic to macronormoblastic with the production of thin macrocytes. Perhaps hepatic disease may affect erythrocyte maturation by interfering with the normal utilization of erythropoietic factors. The marrow alteration and thin macrocytosis persist until the liver heals (Fig. 3d).

THICK MACROCYTOSIS

Thick macrocytosis is a condition in which both thick and thin macrocytes are present in the blood stream, the thick macrocytes being present in sufficient numbers to raise the mean cell volume to 110 cubic microns (μ^3) or more. It is the least common type of macrocytosis and was found in only 17 patients, or 12% of our patients with macrocytosis (Fig. 1 and Table I).

Blood and Bone Marrow Picture

The blood picture is bizzare and has a striking resemblance to that of untreated pernicious anemia (Fig. 1 and Table II, column C). The blood contains large, obese, round or oval macrocytes, thin macrocytes, microcytes, poikilocytes and giant polymorphonuclear leukocytes and shows marked anisocytosis. The mean cell volume is elevated sometimes to high levels. Anemia is usually marked.

Erythroid maturation in the bone marrow is megaloblastic in those with an erythrocyte count below 2 million, atypical megaloblastic in those with an erythrocyte count between 2 and 3.5 million, and macronormoblastic in those with a higher count.

Comparison with Pernicious Anemia

The similarity between the blood and bone marrow of patients with thick macrocytosis of hepatic disease and those of patients with pernicious anemia has been mentioned. What is the relation between the two diseases?

In pernicious anemia the morphologic characteristics of the blood and bone marrow vary with the erythrocyte count. When the erythrocyte count is low (2 million or less) the classic blood picture and megaloblastic marrow are seen. With a higher erythrocyte count (2 to 3.5 million) the blood picture is still macrocytic but not as bizarre; the mean cell volume is lower although still above 110 μ^3 and the bone marrow picture is atypical megaloblastic. When the erythrocyte count is above 3.5 million, as found in patients who have received enough treatment to correct the anemia but not to eliminate the macrocytosis, or in patients in early relapse, the blood picture is again different. These patients have broad, thin macrocytes, very little anisocytosis, a mean cell volume below 110 μ^3 and a macronormoblastic marrow.

The blood and bone marrow films of patients with the thick macrocytosis of hepatic disease were

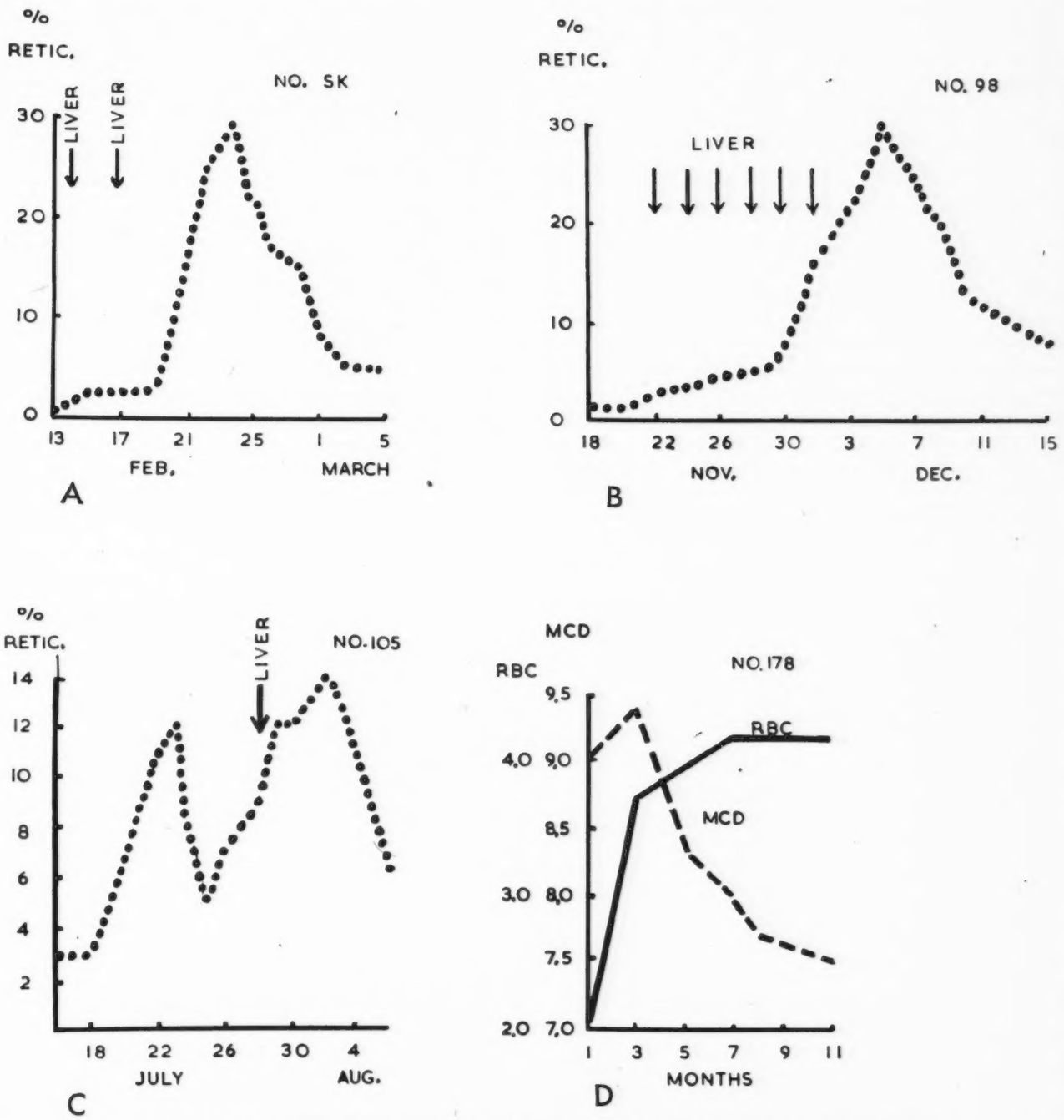


Fig. 3.—(a) The reticulocyte response of a patient with thick macrocytosis to the administration of liver. (b) The delayed peak of the reticulocyte response to the administration of liver of a patient with thick macrocytosis. (c) The reticulocyte response to diet alone of a patient with thick macrocytosis. (d) This patient originally had thick macrocytosis which rapidly disappeared after correction of the malnutrition. The co-existing thin macrocytosis was unaffected by food but gradually disappeared over several months with healing of the underlying hepatic disease.

similar to the blood and bone marrow films of patients with pernicious anemia and a low erythrocyte count.[3] In each were thick obese macrocytes, microcytes, poikilocytes, marked anisocytosis, high mean cell volume, giant leukocytes, severe anemia and megaloblastic or atypical megaloblastic maturation.

The blood and bone marrow films of patients with the thin macrocytosis of hepatic disease were similar to the blood and bone marrow films of patients with pernicious anemia and a high erythrocyte count.[3] In both diseases there were broad thin macrocytes, normal mean cell volume, normal leukocytes, little anemia and macronormoblastic marrow.

Despite the similarity between the macrocytosis of hepatic disease and the macrocytosis of pernicious anemia, the two were not the same. The following differences were observed.

1. At comparable erythrocyte levels patients with pernicious anemia showed greater immaturity in the blood and bone marrow and greater anisocytosis in the blood than did patients with hepatic disease. For instance, the blood and bone marrow

of a patient with pernicious anemia and an erythrocyte count of two million was comparable to that of a patient with hepatic disease and an erythrocyte count of 1.5 million. No patient with hepatic disease had the extreme blood and bone marrow changes found in the patient with pernicious anemia and a very low erythrocyte count of 1 million or less.

2. Free hydrochloric acid was present in the gastric secretion of all the patients with thick macrocytosis of hepatic disease.

3. The administration of vitamin B_{12} (100 μg. or more, weekly by parenteral injection) to three patients did not produce a reticulocyte response or disappearance of thick macrocytosis. The administration of concentrated liver extract (40 units or more, weekly by parenteral injection) to five patients produced a reticulocyte rise and a disappearance of thick macrocytes (Fig. 3a, b). The height of the reticulocyte response was that expected in pernicious anemia but the curve was different. Some patients had a delayed peak to their reticulocyte curve while others had a delayed fall from the peak (Fig. 3b).

4. Diet alone produced a satisfactory reticulocyte rise and disappearance of thick macrocytosis in some patients (Fig. 3c).

Dietary Deficiency

Thick macrocytosis was found only in patients with one of two diseases, each of which was accompanied by malnutrition. The first included patients with chronic alcoholism who had a long history of severe food deprivation prior to admission to hospital and the second included patients with subacute yellow atrophy of the liver who lingered for long periods between life and death without eating (Fig. 2).

The nutritional values of the pre-hospital diets of patients with Laennec's cirrhosis and alcoholism were compared with the type of macrocytosis present. Thick macrocytosis was found in patients with a severe dietary deficiency whereas the presence or absence of thin and/or target macrocytosis was unrelated to diet.[3]

Thick macrocytosis appeared to be caused by a dietary deficiency which markedly altered erythrocyte maturation in the bone marrow so that thick macrocytes were produced. However, not all patients with this degree of dietary deficiency developed thick macrocytosis. In searching for the explanation of this discrepancy the importance of pre-existing hepatic parenchymal cell damage, macronormoblastic maturation and thin macrocytosis was recognized. The patient who already had these changes seemed more vulnerable to malnutrition than one who had not. Malnutrition in the former might be followed by megaloblastic or atypical megaloblastic maturation and thick macrocytosis, whereas in the latter it might give rise to hepatic parenchymal cell damage, macronormoblastic maturation and thin macrocytosis. When a patient with thick macrocytosis ate a balanced diet, the bone marrow rapidly reverted to macronormoblastic maturation and the thick macrocytes disappeared. The pre-existing thin macrocytes persisted, however, until the underlying hepatic disease was healed (Fig. 3d).

TARGET MACROCYTOSIS

The target cell is an exaggerated form of thin macrocyte. Its diameter is greater and its thickness less than that of the other thin macrocytes in the blood film (see below). Viewed on its flat surface there is a central core of hemoglobin, surrounded by a transparent ring and finally a peripheral ring of hemoglobin which gives the cell the appearance of a target (Fig. 1).

Target cells were first described in 1933 by Haden and Evans[10] in cases of sickle cell anemia. The first mention of target cells in hepato-biliary disease was by Barrett[11] in 1934 who found them in patients with biliary tract obstruction. In 1943 Greenblatt and Kaplan[12] described them in soldiers with hepatitis and jaundice. Barrett[11] found that target cells had decreased fragility to saline, indicating that they were flat cells. Valentine and Neel[13] produced target cells by suspending normal erythrocytes in hypertonic plasma or serum; they also converted naturally occurring target cells to normal cells by suspending them in plasma rendered hypotonic by dilution with distilled water. Dacie[14] studied a patient whose spleen had been removed and whose erythrocytes all contained iron-staining inclusion bodies. When this patient was given transfusions during an attack of hepatitis, the donor erythrocytes, which contained no inclusion bodies, became target cells. This observation suggested to him that target cells arose through changes in normal cells in the peripheral circulation.

Frequency of Target Cells

One hundred and twenty patients (54% of the 222 patients) had target cells in their blood. While most patients had only the occasional target cell, 47 patients had from 10% to 50% target cells. Of these 47 patients, 39 had erythrocytes with a mean cell diameter of 7.60 μ or more and they had, by definition, target macrocytosis; five patients had sufficient macrocytes to increase anisocytosis above the normal figure of 0.56 μ but not to increase the mean cell diameter above normal; three patients had small flat erythrocytes with only the occasional macrocyte. To conform with the presentation of the other two types of macrocytosis, only the 39 patients with macrocytosis and 10% or more target cells should be included in this discussion. However, as the cause of the target cells of the eight patients without macrocytosis was the same as that of the 39 patients with macrocytosis, they have been combined into one group.

Blood and Bone Marrow Picture

No distinctive blood picture accompanied the presence of target cells. Of the 39 patients with target macrocytosis 35 had an underlying blood picture of thin macrocytosis and four of thick macrocytosis.

The presence of target cells was not accompanied by any specific changes in the bone marrow. Eighteen iliac marrow aspirations were obtained from patients with target macrocytosis. Seventeen showed macronormoblastic maturation and one showed atypical megaloblastic maturation (a patient with thick macrocytosis).

Origin of Target Cells

The patients with target cells fell into two groups: those with large numbers and those with only the occasional target cell. The target cells of patients in the first group (10% or more) were found to arise from a further flattening of thin macrocytes, or thin erythrocytes, caused by prolonged and severe obstruction to the flow of bile. The reason for the presence of only the occasional target cell was undetermined. An occasional target cell occurs in many disorders and it was impossible to attach much significance to its presence in patients with hepato-biliary disease.

The evidence that the target cell arises from a thin macrocyte or a thin erythrocyte through a process of further flattening is as follows:

1. Thin macrocytes or thin erythrocytes were present in the blood of all patients with 10% or more target cells. Target cells could be seen to arise out of these thin cells. One could easily trace, in serial blood films, the transformation of the thin macrocyte or thin erythrocyte into the target cell. The first change noted was the appearance of a pale area in the centre of the previously homogeneous thin cell, giving the appearance of marked hypochromia. This was not true hypochromia, as the mean cell hemoglobin concentration was normal in the majority of the patients with target cells (Table II). Next a bud of hemoglobin appeared on the inside of the peripheral ring of hemoglobin. The bud of hemoglobin then separated from the peripheral ring and became the central core, thus completing the target cell appearance. The reverse process was also observed. As jaundice disappeared, the target cells were seen to change back into thin macrocytes.

2. Target cells were broader and thinner than other non-target thin macrocytes in the blood, which suggests that they arose from the latter by a process of further flattening. Examples of the increased diameter of target cells are shown in Table III. The decreased thickness of target cells could only be shown indirectly. If the greater diameter of target cells was accompanied by greater thickness, such as would occur if target cells were actually larger cells, the mean cell thickness of all the erythrocytes would increase proportionately to the number of target cells present. This was not found. The mean cell thickness of blood which contained from 10% to 50% target cells was not increased but rather, if anything, was decreased (Table IV). This was interpreted to mean that the target cells were thinner than other non-target erythrocytes of the same diameter.

TABLE III.—COMPARISON BETWEEN MEAN CELL DIAMETER OF NON-TARGET CELLS AND TARGET CELLS OF FOUR PATIENTS WHOSE BLOOD CONTAINED OVER 10% TARGET CELLS

Patient's file No.	*Mean cell diameter of target cells (μ)*	*Mean cell diameter of non-target cells (μ)*
103	8.14	7.68
114	8.95	7.95
171	7.95	7.67
241 (a)	8.32	8.26
241 (b)	7.74	7.19

Two hundred target and 200 non-target cells were measured in each patient.

TABLE IV.—COMPARISON BETWEEN MEAN CELL THICKNESS (MCT) OF ERYTHROCYTES OF PATIENTS WITHOUT TARGET CELLS AND WITH 10% OR MORE TARGET CELLS AT COMPARABLE BUT VARYING MEAN CELL DIAMETER

Mean cell diameter (μ)	*MCT of patients without target cells (μ)*	*MCT of patients with target cells (μ)*
Below 7.60	2.30 (62)	2.36 (8)
7.60 - 7.99	2.10 (39)	2.08 (19)
8.00 or more	1.91 (29)	1.84 (17)

The numbers in parentheses refer to the number of patients.

The conclusion that obstruction to the flow of bile transforms the thin macrocyte or thin erythrocyte into the target cell, and that this change takes place in the peripheral circulation is based on the following evidence:

1. Target cells were found relatively more commonly in the presence of those diseases in which prolonged and severe jaundice was the outstanding feature, such as cancer (of the liver, bile passages or head of pancreas) and biliary cirrhosis (Fig. 2). Patients with other forms of hepato-biliary disease usually did not develop target cells until severe jaundice appeared. Severe jaundice has been defined as jaundice with a van den Bergh reading of 15 units or more, present for 14 days or more. Target cells were found in none of the 10 patients with uncomplicated stone in the common bile duct, doubtless because of the short duration of their jaundice. However, target cells were found in a patient with a stone in the common bile duct and prolonged obstruction to the flow of bile causing biliary cirrhosis.

2. The correlation between the presence of jaundice and target cells is shown in Table V. The correlation between severe jaundice and 10% or more target cells is shown in Fig. 4.

Canad. M. A. J.
July 22, 1961, vol. 85

TABLE V.—THE RELATION BETWEEN THE FREQUENCY OF TARGET CELLS AND THE PRESENCE OF THE PHYSICAL SIGNS OF HEPATIC DISEASE

	No. without target cells	*No. with less than 10% target cells*	*No. with 10% or more target cells*	χ^2*	*p*
Jaundice	60	50	45	19.8	<.001
Spider nevi	34	18	9	5.0	>.05
Hepatomegaly	69	54	36	3.4	>.10
Splenomegaly	31	14	4	11.2	<.01
Ascites and/or edema	35	32	13	4.2	<.20

The figures refer to numbers of patients.

*The chi square and corresponding probability value indicate whether or not the distribution of patients according to frequency of target cells in the case of each sign differs significantly from the distribution in the case of all patients without the sign. For example, in the case of jaundice there were 60 patients with no target cells, 50 with less than 10% and 45 with more than 10%, as compared with 169, 118, and 62, respectively, in the case of patients without jaundice.

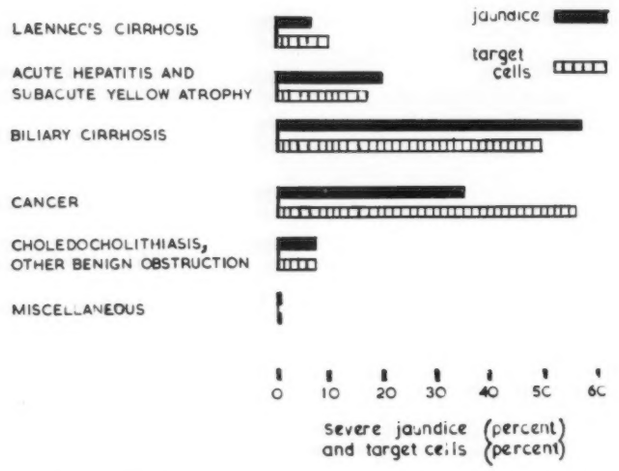
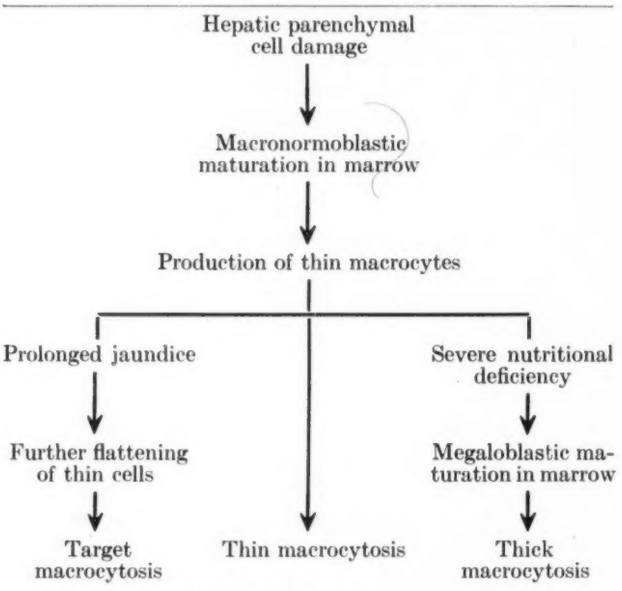


Fig. 4.—This figure shows that for each type of hepatobiliary disease the percentage of patients with 10% or more target cells parallels the percentage of patients with severe jaundice.

3. The most convincing evidence for the importance of biliary obstruction in the etiology of target cells was the disappearance of target cells when such obstruction was relieved. Four patients with target cells had obstructive jaundice caused by the following: cancer of the head of the pancreas (patients 1 and 2); chronic pancreatitis (patient 3); fibrosis of the common bile duct and biliary cirrhosis (patient 4). The jaundice was relieved by cholecystoduodenostomy in patients 1, 2 and 3 and by the insertion of a T-tube into the common bile duct of patient 4. These palliative procedures did not alter the underlying condition but did relieve the obstruction to the flow of bile. With relief of jaundice the target cells in the blood either disappeared or markedly decreased. The thin macrocytes, also present in large numbers, persisted unchanged. The target cells of patient 1 did not entirely disappear because the biliary obstruction was not completely relieved as shown by the persistence of mild jaundice. After the insertion of the T-tube in patient 4 the number of target cells increased for 10 days because of a delay in the flow of bile through the T-tube. As the bile flowed through the T-tube on the seventh day the target cells rapidly disappeared. This demonstrated that it was the relief of the obstruction which resulted in the disappearance of target cells.

The change of thin macrocytes into target cells and back again could be easily followed by inspection of serial blood films. These changes, plus the speed with which they occurred, supported the belief that target cells arose in the peripheral circulation. Further evidence for this belief was the observation that the nucleated erythrocytes in the bone marrow of patients with target cells were the same size as the nucleated erythrocytes of patients with a comparable blood picture but no target cells. The larger target cells were not produced by larger bone marrow cells.

TABLE VI.—THE EVOLUTION OF THIN, THICK AND TARGET MACROCYTOSIS



The evolution of target macrocytosis compared with the evolution of thin and thick macrocytosis is summed up in Table VI.

SUMMARY

A macrocytic blood picture (mean cell diameter 7.60 μ or more) was found in 62% of 222 patients with various types of hepatic and biliary tract disease.

Three different types of macrocyte were present in the blood films: a thin macrocyte, a thick macrocyte and a target macrocyte. Macrocytosis has been defined according to the predominant macrocyte present: thin macrocytosis, thick macrocytosis and target macrocytosis.

Thin macrocytosis is the type of macrocytosis in which all of the macrocytes are thin. Thick macrocytosis is the type of macrocytosis in which both thick and thin macrocytes occur, the thick macrocytes being present in sufficient numbers to raise the mean cell volume to 110 μ^3 or greater. Target macrocytosis is

that type of macrocytosis in which 10% or more of the macrocytes show target cell changes.

Thin macrocytosis is caused by a macronormoblastic type of erythrocyte maturation in the bone marrow which produces flattened erythroctyes whose diameter is greater and whose thickness is less than the normal erythrocyte, but whose volume is the same. This alteration in erythrocyte maturation follows hepatic disease from any cause, provided hepatic parenchymal cells are damaged. It does not occur in hepato-biliary diseases where hepatic parenchymal cells are not damaged, such as in fatty liver or uncomplicated bile duct obstruction due to a stone. It is not caused by a deficiency of any substance necessary for hematopoiesis and it is not corrected by the administration of folic acid, liver, or vitamin B_{12}. Thin macrocytosis disappears only with healing of the underlying hepatic cell disease.

Thick macrocytosis is caused by nutritional deficiency. Patients who have pre-existing hepatic disease, macronormoblastic maturation and thin macrocytosis are particularly vulnerable to nutritional deficiency. In such patients a serious nutritional deficiency may produce a megaloblastic or atypical megaloblastic maturation and a blood picture closely resembling, but not identical to, untreated pernicious anemia. In patients without pre-existing hepatic disease the same nutritional deficiency may result in only thin macrocytosis. Thick macrocytosis rapidly disappears when a good diet is consumed, but the thin macrocytes also present persist until healing of the hepatic disease is complete.

Target macrocytosis is caused by prolonged biliary obstruction. The severity and duration of the obstruction required to produce target macrocytosis will depend on the presence or absence of pre-existing thin macrocytosis. If thin macrocytosis is present, target macrocytosis may appear as early as two weeks after the onset of jaundice. If thin macrocytosis is absent, the obstruction first causes hepatic cell damage and thin macrocytosis and then target macrocytosis. The thin macrocyte is changed into the target macrocyte by a further flattening and rearrangement of hemoglobin which takes place in the peripheral circulation. Because target macrocytosis is related to prolonged obstruction to the flow of bile, it is found principally in patients suffering from cancer of the head of the pancreas and bile ducts and from biliary cirrhosis.

The author wishes to express his thanks to Professors W. Hurst Brown and R. F. Farquharson, Physician-in-Chief at the Toronto Western Hospital and the Toronto General Hospital, respectively, for permission to study these patients; Dr. J. G. Watt, for supplying most of the measurements for the patients with pernicious anemia; Dr. H. D. Bett, of the Connaught Medical Research Laboratories, for estimating hepatic vitamin B_{12}; and his technician, Mrs. K. A. Salwa, who made most of the measurements.

REFERENCES

1. GRAM, C.: Cited in: *Acta med. scandinav.* (Supp. 220), 132: 1, 1948 (Larsen).
2. BINGHAM, J.: *Blood,* 14: 694, 1959.
3. *Idem*: *Ibid.*, 15: 244, 1960.
4. WINTROBE, M. M.: *Arch. Int. Med.*, 57: 289, 1936.
5. LARSEN, G.: *Acta med. scandinav.* (Supp. 220), 132: 1, 1948.
6. MEULENGRACHT, E. AND GORMSEN, H.: *Blood,* 3: 1416, 1948.
7. ROSENBERG, D. H.: *Am. J. M. Sc.*, 192: 86, 1936.
8. BERK, L.: *J. Clin. Invest.*, 27: 525, 1948 (abstract).
9. HARRIS, J. W. AND SCHILLING, R. F.: *Ibid.*, 29: 820, 1950 (abstract).
10. HADEN, R. L. AND EVANS, F. D.: *Arch. Int. Med.*, 60: 133, 1937.
11. BARRETT, A. M.: *J. Path. & Bact.*, 46: 603, 1938.
12. GREENBLATT, I. J. AND KAPLAN, G.: *J. A. M. A.*, 122: 806, 1943.
13. VALENTINE, W. N. AND NEEL, J. V.: *Am. J. M. Sc.*, 209: 741, 1945.
14. DACIE, J. V.: Quoted by: Crosby, W. H.: *Blood,* 7: 261, 1952.

PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

McGILL'S NEW BUILDING

The new home of the medical faculty of McGill University was formally opened by His Excellency the Governor-General, Lord Grey, who is also the official Visitor of the University, on June 5th, 1911.

The Faculty of Medicine of McGill University is the direct outcome and continuance of a teaching body known as the Montreal Medical Institution, which was organized as a medical school in the years 1823-4 by Drs. Wm. Robertson, Wm. Caldwell, A. F. Holmes, John Stephenson, and H. P. Loedel. These men constituted the first medical staff of the Montreal General Hospital, itself established in 1819. The first session of the Montreal Medical Institution opened in November, 1824, with twenty-five students, and the lectures were given at the house of the institution, No. 20 St. James Street, a building situated on the north side of that street at or near Place d'Armes. In the year 1829, the Montreal Medical Institution became, by the formal act of the governors of the Royal Institution for the Advancement of Learning, the Medical Faculty of McGill University. The first session of the McGill Medical Faculty took place in the winter of 1829-30, and the first university degree, a medical one, was conferred four years later, in 1833.

The work of the faculty was carried on for some years in the centre of the city, until 1872, when a building in the university grounds was provided by the governors. This building met the demands of the steadily increasing number of students until 1885, when an addition was found necessary. In 1893 the late Mr. J. H. R. Molson purchased property adjoining the grounds of the college, and enabled the faculty to erect new buildings, and extensively alter and improve those already in use. The new wings comprised a large, new lecture room capable of accommodating one hundred and fifty students, and new laboratories for pathology, histology, pharmacology, and sanitary science. The library and the museum of pathology were also enlarged and improved, and notwithstanding the greatly increased accommodation, a further extension became almost imperative in less than five years.—*Canad. M. A. J.*, 1: 684, 1911.

Canad. M. A. J.
July 22, 1961, vol. 85

ALPHA-CHYMOTRYPSIN IN CATARACT SURGERY*

G. S. HARRIS, M.D.,† *Toronto*

INTRODUCTION

ABOUT TWO thousand years ago Celsus discovered that vision could be restored to those blind from opacities of the crystalline lens by an operation known as couching. Since that time physicians have evolved the technique of cataract extraction and have been continuously modifying the procedure to improve the results. A new drug which promises to facilitate the operation is alpha-chymotrypsin.

Alpha-chymotrypsin was introduced to the world of ophthalmology by Barraquer[1, 2] of Spain in May 1957. Its property of dissolving the zonule of the lens was discovered somewhat by accident. Barraquer attempted to dissolve blood in a blind eye containing a vitreous hemorrhage by injecting trypsin. Several days later he noted that the lens had spontaneously dislocated. Since that time considerable interest has been evidenced in the possibilities of this new drug and many ophthalmic surgeons have used it during cataract extractions. In the past year alone, in the journals of ophthalmology of the English-speaking world more than 50 articles have been exclusively devoted to the topic of alpha-chymotrypsin.

Alpha-chymotrypsin is an enzyme—an endopeptidase—which was extracted from bovine pancreas by Kunitz and Northrop[3] in 1935. The present product is highly purified by repeated crystallization. It derives its name, chymotrypsin, from its curdling effect on milk, in contrast to trypsin which does not possess such an action. Other chymotrypsins exist, e.g. beta, gamma, epsilon, but the alpha form appears to be the best suited to ocular surgery.

Products from different laboratories may differ depending on the water of crystallization and on the amount of inert content. The drug is assayed by determining the amount of substance required to release one microgram (μg.) of tyrosine from denatured hemoglobin substrate. When used in the standard dilution of 1/5000, 2 mg. is dissolved in 10 ml. of liquid. If ¼ ml. is used, 1/20 mg. will be the amount used for zonulolysis.

The enzymatic action of reconstituted alpha-chymotrypsin may be inactivated or inhibited if the solution is left for more than four days at 25° C.,[4] or by contact of the diluted mixture with alcohol, soaps, detergents, strong alkalis, strong acids and some antiseptics. Antibiotics do not seem to interfere with its activity.

PRESENT STUDY

The present study is concerned with the evaluation of the drug as used in 36 consecutive cataract extractions performed by the author at the Toronto General Hospital. Approximately every second case received alpha-chymotrypsin. These patients were unselected as to age, sex, medical ailments and ocular pathology. They varied in age from 34 to 88 years and their average age was 71 years (Table I). Four of the eyes operated upon were in patients 40 years of age or younger. Accurate records were kept of the factors influencing the operation. These included the patient's general health, ocular disease (Table II), type of operation performed, method of anesthesia, and the use of antibiotics, steroids and mydriatics. Observations were made on the ease of extraction and on such factors as loss of vitreous, rupture of the lens capsule, presence of a broken vitreous face, postoperative reaction, hemorrhage, postoperative flat anterior chamber, retinal or choroidal detachment and infection.

TABLE I.—AGE, SEX AND NUMBER OF CASES

Total number of cases	36
Number receiving alpha-chymotrypsin	20
Age range (years)	34 to 88
Average age (years)	71
Female patients	14
Male patients	22

TABLE II.—ASSOCIATED MEDICAL AND OCULAR FINDINGS

Medical disease	*Number of patients*
Diabetes (controlled)	3
Hyperthyroidism (controlled)	1
Congestive heart failure (controlled)	1
Hepatic cirrhosis	1
Manic depressive psychosis	1
Senile psychosis	1
Syphilis	1
Ocular findings	
Retinitis pigmentosa	2
Corneal dystrophy	2
Duane's syndrome	1
Disciform macular degeneration	1
Keratoconus	1
Uveitis	1

The operations were performed with the assistance of one of the staff ophthalmologists. Routine investigation included a general physical examination, ocular examination, bacteriological studies of the conjunctivae and lid margins and irrigation of the nasolacrimal system. All patients were given erythromycin and sulfisoxazole preoperatively for 12 hours and postoperatively for 48 hours, systemically.

The operative technique varied from case to case. However, one of two basic procedures was used: (a) McLean-type pre-placed sutures with a corneo-scleral keratome incision and limbus-based flap, or (b) Graefe corneal section under a small fornix-based conjunctival flap with post-placed sutures.

*Presented at the University of Toronto Eye Alumni Meeting, Toronto, November 18, 1960.

†Assistant Resident, Department of Ophthalmology, University of Toronto, Toronto.

Anesthesia and akinesia were obtained with van Lint and retrobulbar injections of 2% lidocaine HCl with adrenaline.

The alpha-chymotrypsin was usually injected through a peripheral iridectomy under each side of the iris using a bent lacrimal cannula on a 2-ml. syringe. The 1/5000 dilution of Ringer's solution was made immediately prior to its use. Usually ¼ to ½ ml. was injected, although occasionally as much as 1 ml. was given. The solution was injected with a slight amount of force so that the iris ballooned forward, indicating that the medication had reached the inferior zonular fibres. After three minutes the anterior chamber was irrigated with 5 to 10 ml. of Ringer's solution. If a total iridectomy was contemplated, it was performed at that time. In most cases the lens was tumbled using an erisophake, which was applied after the irrigation of the chamber.

It was felt that, within limits, the amount of alpha-chymotrypsin used was not too important as long as the anterior chamber was well filled. The anterior chamber holds only 0.125 ml. and the minimum amount given was 0.25 ml. Numerous authors mention that the lens is seen to lift up in two to three minutes, as the zonular fibres break. This was not seen, but it was noted that the lens assumed a more spherical appearance under the iris. The ease of extraction, however, suggested that the lens was free of its attachments.

TABLE III.—POSTOPERATIVE COMPLICATIONS

	Without alpha-chymotrypsin		*With alpha-chymotrypsin*	
Complication	*Number*	*% of cases*	*Number*	*% of cases*
Broken capsule	1	6	2	10
Broken vitreous face	3	18	0	0
Postoperative inflammation	5	30	3	15
Hyphema	6	36	2	10
Loss of vitreous	2	12	0	0
Vitreous hemorrhage	0	0	2	10
Striate keratitis temporary	12	75	10	50
permanent	0	0	0	0
Shallow anterior chamber	2	12	0	0
Flat anterior chamber	0	0	2	10
Choroidal detachment	2	12	2	10
Retinal detachment	0	0	0	0
Wound dehiscence	0	0	1	5
Glaucoma (controlled)	1	6	1	5
Infection	0	0	0	0

TABLE IV.—RELATIVE EASE OF EXTRACTION. CASES IN WHICH ALPHA-CHYMOTRYPSIN WAS USED COMPARED WITH THE CONTROL SERIES

Definitely easier	55%
Questionably easier	30%
No easier	15%

Tables III and IV compare the group of patients who received alpha-chymotrypsin with those who did not receive the drug. As the operations have been performed relatively recently, it is possible that further complications may be noted at a later date. Table III lists complications found after cataract extraction and indicates the incidence of operative sequelae for both the control group and the group receiving alpha-chymotrypsin. Table IV illustrates the relative ease of extraction.

DISCUSSION

It can be seen from Table IV that the majority of cataract extractions were considered to be easier when the drug was used. In addition, it was found that less manipulation was necessary in the removal of the lens and the amount of trauma to the globe was reduced. Although some surgeons have felt that the drug increases postoperative reaction in the eye, this was not experienced in this series. The incidence of bulbar injection, uveitis and endothelial changes was reduced in the eyes of those receiving alpha-chymotrypsin. This may be due to the greater purity of the products which are now available. It is wise to avoid manipulation in the anterior chamber as much as possible. It has been reported that although alpha-chymotrypsin does not in itself produce striate keratitis, it may soften the endothelium and make it more vulnerable to abrasion.[5] Early in the series most of the lenses were removed by the tumbling technique, but later it was found quite feasible to slide the lens from the eye with pressure from below, grasping with forceps the upper pole of the lens as it presented.

If the drug is not effective in a given case, an insufficient amount may have been used, it may have been improperly prepared, there may have been minute traces of antiseptic in the syringe, or the drug may have been allowed to become too warm after mixing.

In one of the patients the wound separated 10 days postoperatively. This may have been due to the fact that two sutures of plain gut were used. It is recommended that more sutures be used and that silk or chromic gut be chosen for suture material. However, experimental studies on these latter two materials show no loss of strength after immersion in alpha-chymotrypsin.[6] The patients in this series showed less breakage of the vitreous face, less vitreous loss and fewer hyphemas than are usually noted in routine cataract operative techniques without alpha-chymotrypsin.

It has been reported that this agent should not be used in patients under 16 to 20 years of age, and that probably it is of little value for patients over the age of 65 years.[7]

SUMMARY

Alpha-chymotrypsin has been used in 20 unselected cataract extractions and the results have been compared with those in a similar control group. No particular dangers or complications were noted and it was

felt that the drug facilitated the extraction of the lens, particularly in the younger age group.

The drug used in this study was supplied by The British Drug Houses (Canada) Ltd., Toronto.

REFERENCES

1. BARRAQUER, J.: Zonulolisis enzymatica. Communication a la real Academia de Medicinia de Barcelona, April 1958.
2. *Idem*: Enzymatic zonulolysis. Presented at 65th Congress of the French Ophthalmic Society, Paris, 1958.
3. KUNITZ, M. AND NORTHROP, J. H.: *J. Gen. Physiol.*, **18**: 433, 1935.
4. WATTS, L. F., JR. AND MARTIN, C. J.: *A.M.A. Arch. Ophth.*, **65**: 24, 1961.
5. THORPE, H. E.: *Am. J. Ophth.*, **49**: 531, 1960.
6. ALTAMIRANO, R. AND CALLAHAN, A.: *South. M. J.*, **52**: 1327, 1959.
7. TROUTMAN, R. C.: *Tr. Am. Acad. Ophth.*, **62**: 875, 1958.

CIRRHOSIS OF THE LIVER
OBSERVATIONS ON 75 CASES FROM THE UNIVERSITY OF ALBERTA HOSPITAL, EDMONTON

D. R. AMIES, M.B., B.Ch., *Moose Jaw, Sask.*

CIRRHOSIS of the liver is now the eighth leading cause of death in adults in Canada.[1] In the United States it is the fourth leading cause, after cardiovascular disease and neoplastic and renal disease. Hepatic cirrhosis continues to present diagnostic difficulties, especially in regard to its etiology, and frequently its existence is unsuspected. In order to evaluate the incidence of the disease as encountered at the University of Alberta Hospital, Edmonton, all case records from 1948 to 1958 in which this diagnosis appeared were scrutinized.

MATERIAL

Of 175 charts examined, 75 were selected for further study. The reasons, in order of frequency, for rejecting the remainder and the criteria employed for acceptance of the clinical diagnosis are shown in Table I.

TABLE I.

Reasons for rejection
1. Autopsy diagnosis of minimal disease.
2. Failure to substantiate an earlier provisional diagnosis.
3. Failure to meet criteria for acceptance.
4. Inadequate information on chart.
Criteria for acceptance
1. Histological proof.
2. Obvious hepatic insufficiency in the absence of other causes.
3. Biochemical supporting evidence of marked hepatocellular disease.

Among the 75 cases, the diagnosis was proved histologically in 44.

There were several cases in which the diagnosis appeared to be well supported by the history and clinical findings, but which nevertheless failed to meet the criteria outlined. Such rejected cases serve to emphasize the difficulty in compiling a satisfactory series when the diagnosis of the disease is so dependent upon the clinical awareness of the physician and so hard to define by standard methods of investigation.

The biochemical tests regarded as helpful in assessing each case were serum bilirubin,* cephalin-cholesterol flocculation, thymol turbidity, serum protein level, prothrombin time and its response, when depressed, to the parenteral administration of vitamin K, and bromsulphalein excretion.

ETIOLOGY

A careful attempt was made to correlate the history, physical findings, laboratory data and histology (when available) with an etiological diagnosis.

While the majority of cases were of the portal type and were associated with a history of alcoholism, it was found advisable to divide this group into the categories of "definite", "probable" and "possible" as regards the etiologic factor, alcohol.

Similarly, where a previous history suggesting infectious hepatitis existed, cirrhosis was classified as "definitely" or "possibly" a consequence of that disease. The term "postnecrotic cirrhosis" is avoided, since it implies a well-defined pathological entity. Cardiac cirrhosis was similarly subdivided into "definite" and "possible" groups. In this way, cases of less certain etiology could be compared with those more clearly defined.

Biliary cirrhosis is divided into two groups. "Primary" biliary cirrhosis refers to the intrahepatic type of unknown etiology, while "secondary" biliary cirrhosis denotes all other forms. In this series all cases of secondary biliary cirrhosis were due to extrahepatic obstruction.

RESULTS

As indicated in Fig. 1, there were 33 cases of cirrhosis due to alcoholism, 12 followed infectious hepatitis, 12 were idiopathic, 7 were biliary in type, 5 were associated with cardiac disease, 3 with hemochromatosis and 2 with multiple factors.

*The normal value for this estimation and those that follow is given below.
Serum bilirubin, total (15 minutes): 0.2-1.5 mg. %. Cephalin-cholesterol flocculation: not over 2 plus in 48 hours. Thymol turbidity—0 to 4 units. Serum protein: total, 6.4-7.9; albumin, 3.6-5.4; globulin, 2.5-3.6 g. %. Prothrombin time: not less than 80% of control. Bromsulphalein excretion: less than 10% retention in 45 minutes.

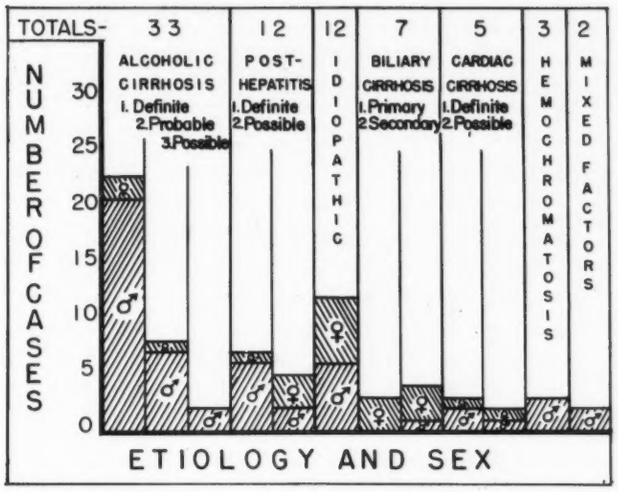


Fig. 1

One case was that of a man who was dead on arrival at hospital; only the autopsy findings were available. This case has not been classified or grouped with the others in the series.

It will be noted that alcoholic cirrhosis is the commonest variety in this series, as it is in other North American centres.[2] There were no recorded cases in association with known exposure to hepatotoxins, with ulcerative colitis, Wilson's disease, thyroid disease or collagen disorders.

Sex Incidence

The male predominance amongst the alcoholic group is striking, as it is also in those with hemochromatosis. In contrast, biliary cirrhosis is more frequent in women, and a large proportion of the cirrhosis following hepatitis is seen in females. The sex ratio in the idiopathic group is equal.

Age Incidence

In the alcoholic group, the ages ranged from 33 to 83 years, but more than one-half of the patients were between 45 and 60 years; the average age was 55.5 years.

The average age for the post-hepatitis group was 42 years, but the range of ages from infancy to senescence renders this figure artificial.

The average age for the idiopathic group was 64.5 years. In this respect an interesting sex difference was noted. The average age for males was 73.5 years and that for females was 55.6 years, the patients of each sex being within a narrow age range, with no overlap of one upon the other.

Presenting Symptoms

The presenting symptoms varied widely from dramatic hematemesis and hepatic coma to the incidental finding of hepatomegaly on routine physical examination. Most patients in the post-hepatitis group could date the onset of their illness accurately to the original episode, while most patients in the alcoholic group had suffered from recurrent episodes of gastrointestinal upset, often with jaundice, for a variable length of time from months to years prior to definite diagnosis. At that stage these patients had lost weight, were chronically ill, sociologically at the lowest ebb of life, and yet somehow managed to maintain an estimated average daily intake of 13 ounces of spirits. There were none whose drinking was confined to beer, but otherwise their drinking habits followed no particular pattern.

Patients with biliary cirrhosis presented with jaundice, often accompanied by pruritus, and with symptoms of the underlying biliary tract disease in "secondary" cases.

Cardiac patients were predominantly sufferers from chronic rheumatic heart disease with tricuspid valvular lesions, or from constrictive pericarditis.

Hemochromatosis presented as diabetes in two instances, and was not detected until autopsy in a third.

Occupation

Occupation appeared to have no bearing on the type of cirrhosis except for that of bartending in the alcoholic group.

Transfusions

None of the patients had received transfusions prior to the development of their disease. Blood groups and Rh types were those of any random segment of the hospital population.

Diet

A strong impression was gained that dietary inadequacy, particularly in respect to protein, was the most important factor in all types of portal cirrhosis. Notoriously difficult to evaluate though it may be, information with regard to diet should be sought in every case.

Physical Signs

The presence of jaundice was noted in 38 cases, in a random distribution, usually when the patient was gravely ill. In biliary cirrhosis, however, deep icterus was compatible with relative well-being. In other cases, jaundice implies marked hepatic insufficiency and is often associated with neurological disorders.

The size of the liver is not an index of the state of its functioning. The occurrence of splenomegaly was only sporadic. Thirteen patients had been in coma at some stage, usually preceded by an interval of personality changes and confusional states, and associated with the classical flapping tremor in each instance.

Blood pressure readings were not significantly lower than those of comparable controls, contrary to the experience of Hall, Olsen and Davis.[3] However, the higher age range in this series may account for this finding.

Canad. M. A. J.
July 22, 1961, vol. 85

CUTANEOUS AND OTHER ASSOCIATED MANIFESTATIONS

These interesting accompaniments of hepatic cirrhosis were recorded as shown in Table II.

TABLE II.—CUTANEOUS AND OTHER ASSOCIATED MANIFESTATIONS

1. Spider nevi (30 cases—19 alcoholic).
2. Palmar erythema (18 cases—11 alcoholic).
3. Loss of hair, testicular atrophy, gynecomastia (5 cases).
4. Petechiae (6 cases).
5. Scratch marks—occasional (jaundice).
6. Venous collaterals (13 cases—9 alcoholic).
7. Digital clubbing (rare).
8. Fingernail changes (nil).
9. Xanthoma (1 case—localized, eyelid).
10. Dupuytren's contracture (nil).

LABORATORY DATA

The serum bilirubin reached its highest levels in cases of secondary biliary cirrhosis, but its precise value did not correspond with any clinical stage, normal values being obtainable when liver function was marginal.

The cephalin-cholesterol flocculation test is affected by so many minor and little understood factors that its interpretation is difficult. However, it may be the only test indicative of abnormality in the latent or subclinical stage of cirrhosis. A value of 2 plus or more in 24 or 48 hours must be regarded with suspicion, since this level of positivity was present in 56 of 64 patients tested, 36 of whom had a level of 3 plus or 4 plus.

The thymol turbidity was only significantly positive in a few cases, mainly in the post-hepatitis group.

The bromsulphalein excretion test is one of the most valuable parameters of liver function, and is one of the most frequently used. The technical and laboratory errors possible are few. In interpreting an abnormal result, it must be remembered that a wide diversity of disorders acting on hepatic blood flow, parenchyma and excretory pathways may interfere with the isolation and excretion of the dye. When bilirubin itself is being retained (i.e. in the presence of even minimal elevation of serum bilirubin), the test is of questionable value.

The prothrombin time was almost invariably low in 59 patients tested, the average result being 52% of normal. In 30 of these the parenteral administration of vitamin K produced no rise in prothrombin levels of 20 patients, while the remaining 10 showed a very slow, insignificant rise which never approached normal. This lack of response appears to be strong evidence of marked generalized liver cell damage.

In regard to plasma protein there was relatively early elevation of the globulin fraction and late hypoalbuminemia, always associated with gross ascites when the albumin concentration was less than 2 g. % in this series. Electrophoretic studies demonstrated a typical "gamma peak" in 14 cases.

The recently available serum glutamic oxaloacetic transaminase test gave results ranging from normal (up to 40 units) to 210 units, and averaged 105 units.

Anemia was not found in any case except where bleeding was a factor, nor was leukocytosis present in the absence of evident infective causes.

Radiological examination with barium disclosed esophageal varices in only 6 of 32 patients, though three old duodenal ulcers and one hiatus hernia were found. Cholecystography and cholangiography are usually unsatisfactory owing to inability of the liver to concentrate the dye. The operative cholangiogram is of value in the investigation of biliary cirrhosis.

MANAGEMENT

While this followed standard methods, analysis of results would be inconclusive in this small series. However, the successful results associated with prolonged hospital care, especially in the reformed alcoholic, are worth mentioning. The latter cases provide some of the best results of therapy, but only if sufficient attention is paid to mental and environmental rehabilitation, and for only as long as the individual remains an abstainer.[4]

Surgery of any kind is most hazardous in the presence of cirrhosis, and is performed only in compelling circumstances. The role of anastomotic operations for the relief of portal hypertension remains a controversial subject in both medical and surgical worlds and will not be discussed here.

PATHOLOGY

The findings from 33 autopsies with histological studies were available. There were two laparotomies to confirm the diagnosis of primary biliary cirrhosis, while wedge biopsy was carried out in three other cases for diagnosis and in a fourth case during the operation of portacaval anastomosis. The diagnosis was substantiated in two patients by needle biopsy. In addition, two autopsies with histological studies were performed at other hospitals, and diagnosis was confirmed in one case by needle biopsy at another centre.

A review of the histological sections revealed the variable degrees of hepatic cell degeneration, regeneration, connective tissue changes and disturbances of architecture characteristic of cirrhosis in general, with the added more specific features of portal, biliary, cardiac and postnecrotic cirrhosis. The latter disorder was rare in its typical form, but coarse nodularity (diameter of nodule more than 13 mm.) with relative preservation of normal architecture within nodules was more frequent.

CONCLUSIONS

The diagnosis of cirrhosis remains primarily a clinical one.

Careful history-taking remains the best method of elucidating etiological factors.

Detailed physical examination may reveal many diagnostic clues.

Laboratory investigation may be negative in the compensated case.

The bromsulphalein retention test must be interpreted with care.

The prothrombin time, and when depressed its response after parenteral administration of vitamin K_1 oxide, is one of the best tests of liver cell function.

Needle biopsy of the liver may be of considerable value in diagnosis and in subsequent follow-up.

Close co-operation between clinician and pathologist in arriving at a final diagnosis, after consideration of all aspects of each case, adds materially to the accuracy and clarity of case records.

SUMMARY

The case histories of 75 patients with hepatic cirrhosis of all types, encountered at the University of Alberta Hospital, Edmonton, in the 10-year period from 1948 to 1958 are reviewed, and an attempt at an etiological diagnosis is made. Various features of interest regarding the incidence, physical signs, laboratory evaluation and histological appearances are discussed.

The author acknowledges with thanks the assistance and advice of Dr. J. A. L. Gilbert, Associate Professor of Medicine, University of Alberta.

REFERENCES

1. CANADA, Dominion Bureau of Statistics, Information Services Division: Canada Year Book 1959, Queen's Printer, Ottawa, p. 213.
2. SUMMERSKILL, W. H. J. *et al.*: *New England J. Med.*, **262**: 1, 1960.
3. HALL, E. M., OLSEN, A. Y. AND DAVIS, F. E.: *Am. J. Path.*, **29**: 993, 1953.
4. SHERLOCK, S.: Diseases of the liver and biliary system, 2nd ed., Charles C Thomas, Springfield, Ill., 1958.

1139 Bogue Avenue,
Moose Jaw, Sask.

EVALUATION OF GUANETHIDINE* IN THE COMPREHENSIVE TREATMENT OF HYPERTENSION
A STUDY OF 25 CASES†

HAROLD Z. POMERANTZ, M.D.,
SIMON BARSKEY, M.D.,
JONATHAN BALLON, M.D.,
GREGORY NEIMAN, M.D. and
ALBERT W. LAPIN, M.D.,
Montreal

GUANETHIDINE was synthetized by Maxwell, Mull and Plummer[1] in 1959. The complete range of its pharmacological activities is still imperfectly understood, but the drug appears to have its main effect at the neuromuscular junction of the efferent sympathetic nerves. Here it interferes in some way with the release of the neurohumoral transmitter or else inhibits its action after release. Unlike ganglion-blocking drugs such as mecamylamine and pentolinium, which block sympathetic and parasympathetic pathways alike, guanethidine does not appreciably affect the parasympathetic system. Theoretically therefore it might be expected to reduce blood pressure as effectively as the ganglion-blockers, with fewer side effects. Published studies have suggested that this is in fact the case.[2]

The following report details our experience with guanethidine in a group of ambulatory hypertensive patients.

*Generously supplied as Ismelin by the Ciba Company Ltd., Montreal.

†From the Department of Medicine and the Cardiac Clinic, Jewish General Hospital, Montreal.

MATERIAL AND METHODS

Twenty-five ambulatory patients attending the hypertension clinic were used in this study. The group consisted of 22 women and three men, ranging in age from 30 to 79 years. Fifteen were under 60 years and 10 over 60. Essential hypertension was diagnosed in 22 cases, chronic pyelonephritis in two, and renal vascular disease in one. Most patients in the group had been attending the clinic for many years, 19 of them for more than five years. As a result they were familiar with the clinic routine and the clinic doctors, and were not unduly excited or upset by the various diagnostic procedures; in addition, their individual reactions were well known to the examining physicians. Routine studies included funduscopic examination, an electrocardiogram (ECG), a six-foot chest radiograph, a blood urea nitrogen determination, assessment of serum electrolytes, an intravenous pyelogram, and urinalysis. Special studies included urinary catecholamine determinations in 10 cases, the Howard test in three and an aortogram in one.

In 21 cases, there was both radiological and electrocardiographic evidence of cardiac enlargement. In two other cases heart size was normal by x-ray, but the ECG showed evidence of left ventricular hypertrophy. The ocular fundi, graded according to the Keith-Wagener classification, were Grade I in three cases, Grade II in 18, Grade III in three and Grade IV in one. The blood urea nitrogen value was normal in all but six patients; in no case was it higher than 30 mg. %.

Previous to this study all 25 patients had been on various combinations of sedatives, thiazides, Rauwolfia derivatives and hydralazine. Fifteen had

TABLE I.—EFFECT OF GUANETHIDINE ON HYPERTENSION

Patient	*Age*	*B.P. before treatment with guanethidine or ganglion-blocking drugs*	*B.P. during treatment with guanethidine*	*Side effects*	*Duration of treatment (months)*	*Average dose of guanethidine (mg./day)*
E.B.	58	230/130	195/105 (l)* 162/100 (s)*	Dizziness 1+ Weakness 1+	4	60
R.G.	57	200/110	165/96 (l) 162/92 (s)	Minimal	4	35
M.K.	47	210/110	165/90 (l) 130/86 (s)	Minimal	4	20
B.G.	71	220/115	200/100 (l) 155/96 (s)	Weakness 2+	4	55
M.K.	65	180/120	185/94 (l) 145/84 (s)	Dizziness 1+ Insomnia	4	30
J.S.	65	230/130	196/94 (l) 160/88 (s)	Dizziness 3+ Sudden syncope (120/80)	6	40
R.G.	63	220/120	180/112 (l) 170/110 (s)	Weakness 3+	6	40
B.S.	67	190/110	155/96 (l) 145/90 (s)	Minimal	4	30
S.N.	54	248/96	230/90 (l) 160/80 (s)	Sudden syncope Severe diarrhea	4	40
W.H.	65	230/130	215/100 (l) 160/88 (s)	Dizziness 2+ Weakness 2+	5	50
A.K.	55	186/110	150/95 (l) 145/90 (s)	Minimal	5	20
D.A.	65	210/120	178/105 (l) 165/96 (s)	Weakness 2+ Dizziness 2+; fell once	4	30
F.P.	70	250/130	180/100 (l) 170/90 (s)	Diarrhea 1+ Dryness of mouth 1+	5	30
H.M.	51	230/130	150/90 (l) 120/85 (s)	Minimal	4	20
B.V.	32	200/110	190/100 (l) 150/90 (s)	Weakness 2+ Dizziness 2+	6	20
G.S.	71	210/110	170/100 (l) 160/90 (s)	Dizziness 1+	6	50
I.W.	73	220/110	190/105 (l) 180/100 (s)	Weakness 3+ Dizziness 3+	4	25
T.M.	68	190/110	130/75 (l) 140/70 (s)	Dizziness 3+ Weakness 3+	2	25
F.B.	58	180/110	180/110 (l) 148/100 (s)	Cerebral insufficiency	3½	40
A.K.	57	200/120	180/100 (l) 150/90 (s)	Minimal	5	10
S.B.	79	210/110	170/100 (l) 150/90 (s)	Minimal	5	10
B.Y.	60	220/100	200/90 (l) 190/90 (s)	Weakness 3+ Dizziness 3+	4	37.5
R.B.	40	250/140	150/100 (l) 140/90 (s)	Weakness 1+ Dizziness 1+ Insomnia	3	40
I.J.	44	220/120	190/105 (l) 160/100 (s)	Weakness 3+ Dizziness 3+	3	40
M.B.	58	210/105	200/100 (l) 190/100 (s)	Dizziness 1+ Weakness 1+	2	20

*l = lying B.P. s = standing B.P.

been receiving ganglion-blocking drugs in addition. The ganglion-blocking drugs were discontinued, but all other "background" antihypertensive drugs were continued, as they were in the remaining 10 cases. Guanethidine was then added in small increments to the basic regimen in all 25 cases.

Duration of treatment with guanethidine was between four and six months in 20 cases and between two and three months in 5 cases. The dose of guanethidine varied between 10 and 62.5 mg. per day; the average for all subjects was 30 mg. per day.

RESULTS

Table I summarizes the results obtained. Column 3 gives the control blood pressure in each case. The figure shown represents the average of three or more weekly recordings at a time when the patient was receiving no antihypertensive drugs. Column 4 shows the effect of treatment with guanethidine. The figure shown is the average of three or more weekly blood pressure readings during the period of optimal control. It represents the lowest pressures that could be maintained in each case with due regard to the safety and comfort of the patient. It does not necessarily include the lowest blood pressures achieved with a large dose which had to be reduced subsequently because of severe side effects.

patients experienced sudden staggering and fell without any recognizable warning in the form of increasing dizziness or faintness. Bruises were suffered by all three. Two other patients had momentary blurring of vision associated with severe dizziness. There were no complaints of impotence or failure of ejaculation in the three males included in the study.

Table II summarizes the results obtained with guanethidine compared with those obtained with ganglion-blocking drugs in the 15 cases considered suitable for comparison. There was little difference in hypotensive effects between the guanethidine and the ganglion-blocking drugs, but patients complained less of unpleasant side effects while on guanethidine, and the physicians found the drug simpler and safer to handle.

DISCUSSION

It is generally conceded that sustained hypertension predisposes to cerebral, cardiac and renal complications, and most observers believe that these complications can be prevented or minimized if the blood pressure can be reduced to levels near the normal range and maintained there. In mild and moderate cases satisfactory reduction can usually be achieved by administration of combinations of sedatives, Rauwolfia compounds, hydralazine, and saluretic drugs, and in our opinion there is

TABLE II.—OPTIMAL BLOOD PRESSURE READINGS DURING TREATMENT WITH GUANETHIDINE COMPARED WITH OPTIMAL BLOOD PRESSURE READINGS WITH GANGLION-BLOCKING DRUGS (PENTOLINIUM, MECAMYLAMINE AND PEMPIDINE)

		PATIENT														
		R.G.	*M.K.*	*M.Ko.*	*J.S.*	*R.G.*	*B.S.*	*S.N.*	*F.P.*	*H.M.*	*I.W.*	*A.K.*	*S.B.*	*W.H.*	*R.B.*	*B.G.*
B.P. during treatment with ganglion-blocking drugs	l*	170/100	180/100	176/110	180/105	180/110	170/100	230/95	210/120	150/100	200/105	170/90	170/86	225/112	160/105	210/110
	s*	160/90	150/90	160/90	160/95	175/108	160/98	220/90	190/120	140/90	190/100	140/90	150/80	170/95	150/100	190/100
B.P. during treatment with guanethidine	l*	160/96	165/90	185/94	196/94	180/112	155/96	230/90	180/100	150/90	190/105	160/100	170/100	215/100	150/100	200/100
	s*	160/92	130/86	145/84	160/88	170/110	145/90	220/80	170/90	120/85	180/100	150/90	160/90	160/88	140/90	150/96

*l = lying B.P. s = standing B.P.

It will be seen that during therapy with guanethidine, some degree of reduction in blood pressure over control values was achieved in all 25 cases, especially with the patient in the upright position. In five patients the drop was slight but in 20 the systolic pressure was reduced by 25 mm. Hg or more and the diastolic by 15 mm. Hg or more. In several cases the pressure dropped to near-normal levels. Tolerance to guanethidine—that is, the need to increase the dose to maintain a given effect—was not observed during the period of the study.

Side effects included dizziness, weakness, syncope, dryness of the mouth, epigastric distress and diarrhea. Weakness, dizziness and diarrhea were the most frequent complaints. The diarrhea could usually be controlled by belladonna or codeine or any of the simple conventional preparations, and was never sufficiently severe to require discontinuance of the drug. Sudden faintness, blackouts and syncope were more serious complications. Three seldom an indication for using either guanethidine or ganglion-blocking drugs in such cases.

In more severe cases in which the blood pressure is very high it may be necessary to use the more potent drugs while recognizing fully their unpleasant and potentially dangerous side effects and weighing this against the greater danger of allowing the disease to advance unchecked. Guanethidine shares with the ganglion-blockers the risk of producing sudden dizziness, blackout or syncope, with consequent serious injury, and must therefore be used with appropriate caution. Unlike the ganglion-blockers, it does not cause constipation or urinary retention or extreme mouth dryness. As a result, most patients showed a decided preference for guanethidine over the ganglion-blockers. In order to keep the actual dosage and therefore the side effects to a minimum, it seems to us desirable to prescribe guanethidine in combination with Rauwolfia and thiazide derivatives, and perhaps in

certain cases, even with small amounts of the ganglion-blocking agents.

Certain authors have reported the use of larger doses of guanethidine than were used in this study. In our series we were unable to prescribe more than 62.5 mg. per day without the occurrence of severe side effects; our average dose was 30 mg. per day. In certain of our patients with definite coronary disease, even when obvious side effects were absent, we were unwilling to attempt too great or too abrupt a reduction of blood pressure even if we could have attained it.

SUMMARY

Twenty-five patients with severe hypertension were treated in the Hypertension Clinic at the Jewish General Hospital, Montreal, with guanethidine for two to six months.

A satisfactory sustained drop in systolic and diastolic blood pressure was achieved in 20 of the cases. This drop in blood pressure was usually more marked in the upright position.

Side effects were minimal in seven cases and moderate in 18 cases, but were troublesome and potentially dangerous in a few. Both patients and doctors found guanethidine preferable to the group of ganglion-blocking drugs.

As a general rule, guanethidine should not be prescribed as the sole hypotensive agent and should not be used in the milder cases of hypertension.

REFERENCES

1. MAXWELL, R. A., MULL, R. P. AND PLUMMER, A. J.: *Experientia*, **15**: 267, 1959.
2. PIGEON, G. *et al.*: *Canad. M. A. J.*, **83**: 690, 1960.

SPECIAL ARTICLE

THE VANCOUVER HEALTH CENTRE FOR CHILDREN: EVOLUTION OF THE OUTPATIENT DEPARTMENT DURING A TEN-YEAR PERIOD

GEOFFREY C. ROBINSON, M.D., F.R.C.P.[C]*
and JEAN M. MACLENNAN, M.D., D.P.H.,†
Vancouver, B.C.

TEN YEARS ago Paterson[1] described the development of the Health Centre for Children in connection with the Vancouver General Hospital. He stated that "its purpose should be to act as a consultative centre where advice can be sought on both the preventive and curative sides of children's diseases in all their aspects. It is this close linking together of these fundamental aspects of child health under one roof which we wish to stress and which are essential if the centre is to be a success." He advocated the need for affiliation with a modern, well-equipped hospital, preferably a university medical school, and stressed the importance of integrating the health centre with the community services, particularly the public health nursing and social welfare departments.

In 1954 this outpatient service and the inpatient facilities at the Vancouver General Hospital were brought together in a converted hospital building and together they were named the Health Centre for Children. The outpatient department occupies part of the ground floor of this building, and carries on the functions described in Paterson's paper. The Department of Pediatrics of the University of British Columbia was also located in this building, and one of us (G.C.R.) was named Medical Director of the Outpatient Department when the founder resigned in 1954.

During the ten-year period the Health Centre for Children has continued to develop, and this growth has been stimulated by the establishment of the Medical School at the University of British Columbia in 1951.

The purpose of this report is to describe the outpatient unit at the present time and then to discuss its function and contribution with regard to both community service and medical education.

DESCRIPTION OF THE UNIT

The outpatient department is located on the ground floor of the Health Centre for Children. The medical unit consists of eight small examining rooms, a treatment room and a nurses' room for measuring and weighing the patients. There is one room which serves many purposes, including specialty clinics, teaching, psychological examinations and conferences; and special areas designed to accommodate the needs of the Eye Clinic, the Speech and Hearing Clinic, and the Dental Clinic. In addition, there are individual offices for the medical, nursing, public health, social work and clerical staff, surrounding a central area which serves as a reception and waiting area.

The outpatient program is directed by a member of the Pediatric Department of the Medical Faculty, and his office is located in the department. Two pediatricians, one full-time and one part-time at

*Assistant Professor, Department of Pediatrics, University of British Columbia; Medical Director, Outpatient Department, Health Centre for Children.
†Clinical Instructor, Department of Pediatrics, University of British Columbia.

present, conduct and supervise the offices in the General Medical Clinic.

Various physicians and surgeons, all of whom are members of the Medical Faculty and many of whom serve on a voluntary basis, conduct pediatric or specialty clinics or participate in the management of complex medical problems.

The resident medical staff of the Health Centre for Children receive part of their training in the department. The fourth-year class of the Medical School devote half their time to outpatient medicine during a five-week pediatric experience.

The effective operation of the outpatient department requires the services of laboratories, an x-ray department, and a variety of non-medical specialists to complete diagnostic evaluation and work out realistic treatment and education plans. Included in this latter group are social workers and public health nurses, psychologists, speech and hearing therapists, audiometrists, orthoptists, dietitians, dentists and a geneticist.

The pediatric outpatient services in British Columbia are confined to a financially eligible group of families, which excludes all families insured by approved prepaid medical schemes.* Within these financial limits, our patients separate into two groups; first, the families in adjacent housing areas, many of whom lack a family physician, and second, children with particular problems of diagnosis or management from all areas of British Columbia.

Children with multiple problems, particularly when they are associated with delayed development and require special educational planning, or when social or emotional problems coexist, receive co-ordinated study by various disciplines.

Sound clerical administration is required to arrange a series of appointments for such children. The duration of the outpatient study should be as brief as possible, and this is difficult when some of the staff are only available at fixed times each week. Therefore a good deal of organization is required to bring a family to the outpatient department and to effect adequate study, planning and interpretation to child and parents and to referring physician and community resource.

OUTPATIENT PROCEDURE

The outpatient department provides ambulatory care for children up to their 16th birthday. Acute medical and surgical emergencies are referred to the emergency department of the Vancouver General Hospital. The outpatient program functions five days a week from 8.30 a.m. to 5 p.m.

All the clinics operate on an appointment system. The smooth running of the appointment system is dependent on a number of variables, not all of which are under department control, but such arrangement enhances both medical service and student teaching.

Children are referred to the department by their family physicians, provincial and metropolitan health units, and other social agencies. Appointments for children with acute illness are given by phone, and a written referral is requested in all problems of a chronic nature. Printed referral forms are available for family physicians on request, and the health units complete similar referral forms, in duplicate.

The correspondence relative to children with chronic problems, either single or multiple, is reviewed by the medical director, the social work supervisor, the head nurse and the public health nurse, in an effort to plan suitable appointments for each child. Reports from other hospitals, outpatient departments and social agencies are collected before appointments are arranged, thereby avoiding needless duplication of study and shortening the family stay. The final appointments are reviewed at a weekly staff intake meeting, with the clerical supervisor in attendance, and these are forwarded to the referring physician or agency. During the planning period, the local health nurse or social worker assists with arrangements for travel expenses and accommodation near the Health Centre for Children and in obtaining financial assistance for these matters. The British Columbia Society for Crippled Children operates a hostel (Easter Seal House) less than a block away from the Health Centre for Children, where room and kitchenette facilities are available for families attending the outpatient department.

New patients are first examined in the medical clinic. Patients with specific problems, cardiac, orthopedic and eye defects, are referred to special clinics for consultation or for continuing care. In addition, there are a number of children with particular problems necessitating multiple appointments to various clinics. The latter are assigned, during the assessment period, to a pediatrician who is responsible for integrating the findings of the various professional consultants and interpreting these findings to the family and referring physician. Great effort and skill are required to establish and maintain satisfactory long-term management in these cases.

Many families do not avail themselves of such opportunities or if they do, they fail to follow through with recommendations in a consistent fashion. Incorrect diagnostic work, unrealistic planning, lack of parental acceptance of diagnosis and disability, social and economic distress and social mobility are some of the many causes which prevent children from receiving adequate continuing care and thus deriving maximum benefit from the various resources available in their communities. To strengthen the liaison between the diagnostic resource and the child's community, the public health nurse and social workers in the Health Centre for Children devote considerable time to

*In one area of child health, namely language and communication disorders in preschool children, the financial restrictions are waived as the outpatient facilities are unequalled elsewhere in the community.

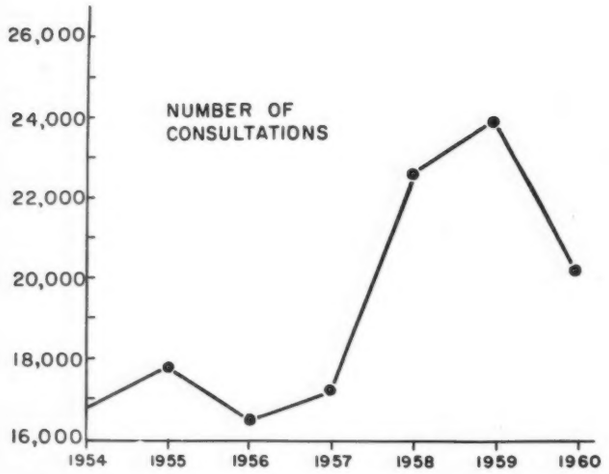


Fig. 1.—Total number of consultations during the years 1954 to 1960 inclusive.

the improvement of this aspect of child care. The family physician and community resources are informed of the department's recommendations in written reports.

The total number of consultations for each of the past seven years is seen in Fig. 1. These consultations can be further divided into three groups, according to the clinic from which they were provided (Medical, Surgical and Specialty Clinics), and these are shown in Table I. Allergy, Dermatology, Cardiology and Neurology are the busy medical clinics, and Ear, Nose and Throat, Ophthalmology and Orthopedics are the busy surgical clinics. Speech and Hearing, Refraction and Orthoptics, and Social Work comprise the bulk of the work in the specialty clinics. The dental consultations were significantly reduced in 1960 owing to lack of staff.

TABLE I.—CONSULTATIONS PROVIDED BY THE MEDICAL, SURGICAL AND SPECIALTY CLINICS IN THE OUTPATIENT DEPARTMENT OF THE HEALTH CENTRE FOR CHILDREN DURING 1960

Medical clinics:	
General Medical	5147
Special Medical	2725
	7872
Surgical clinics:	
Eye	1489
Ear, nose and throat	1135
Others	844
	3468
Specialty clinics:	
Speech and hearing	3684
Refractions and orthoptics	1840
Social work	2048
Others	1121
	8693

The daily number of appointments to each clinic is limited and the number of clinic visits is controlled. The decrease in total consultations in 1960 was designed to improve standards of care within the limitations imposed by space and staff.

COMMUNITY SERVICES

"The focus of pediatric practice has shifted in some countries from the sick child to child health (Puericulture) as a result of reductions in childhood mortality and morbidity."[2] In British Columbia the paramount importance of psychological and social environmental factors in pediatric practice is becoming recognized.

Metropolitan and provincial health departments support extensive programs for care and supervision of well children, and there is an increasing interest in the area of mental health services for children.[3, 4] Our role in child health facilities in British Columbia will be clarified by an explanation of the evolution of these services.

During the past twenty to thirty years, services have developed for diagnosis and management of children with handicaps.[5] Some of these are operated by government departments and others by voluntary societies. For the most part these agencies have identified their function with a particular type of medical problem (mental health, poliomyelitis, tuberculosis, mental retardation, cerebral palsy and blindness) and gradually many of these community medical problems have been reduced. There remain, nevertheless, major unmet needs in the community, such as language and communication disorders and multiple handicaps, and these have been the special concern of the Health Centre for Children.

The outpatient department serves two distinct and separate pediatric functions in the community. The first comprises the routine care of children from the adjacent neighbourhood comparable to the office practice of the general practitioner. With proper supervision considerable responsibility can be given to the medical student or house physician in the medical care of these children. The continued expansion of the prepaid medical schemes in Canada could eliminate this type of experience, comparable to the disappearance of dispensary practice under the National Health Service in the United Kingdom. On the other hand, the Edinburgh General Practice Teaching Unit has greatly enhanced the effectiveness of the teaching of medical students.[6]

The second role which this outpatient department plays in the community is a consultative one. The availability of medical and paramedical specialists and diagnostic facilities, both radiological and laboratory, provides a unique setting for the evaluation of difficult problems in children.

There are many children with various handicaps who require a thorough diagnostic evaluation before rehabilitation, recreation and education can be well planned. This is well illustrated by the problems of a child with a cleft palate, who may have surgical, dental, otological and speech problems, and who may well develop psychological and educational problems as he gets older. Evaluation of the child with multiple handicaps demands a wide variety of medical specialists, particularly in

pediatrics, neurology, otology, ophthalmology, cardiology, orthopedics, psychiatry, pediatric radiology and pediatric surgery; and specialists in psychology, orthoptics, speech therapy, audiometry, social work, genetics, dentistry, etc. Field workers, particularly public health nurses, social workers and teachers, provide first-hand information on the home and family relationships and attitudes, which without a home visiting program is not otherwise available to the medical student.

It is well recognized that many such children cannot be effectively studied in hospital and obviously should not be hospitalized. Outpatient investigation may necessitate several days in attendance but the child is spared the added anxiety of separation from the family. We have been able to complete very comprehensive outpatient studies of young children who after hospitalization for two or three weeks had yielded only conflicting findings and regression in behaviour. Various common problems in children, with or without social and emotional complications, are ideally studied on an outpatient basis.

Such diagnostic studies are finalized when the various people involved discuss their findings and agree to a realistic plan of management, which is drawn up with an understanding of the child's home and community. The family physician and the community resources involved are informed of the recommendations of the group.

MEDICAL EDUCATION

Scott in describing the Edinburgh University General Practice Teaching Unit[6] emphasizes that the postwar era was characterized by major changes in orientation, both in teaching and research, in the field of social and preventive medicine. Medical educators everywhere[7] have been exploring a variety of ways of teaching medical students the importance of psychological and social factors in health and disease.

It is interesting that the outpatient department and the house visit are being used more extensively now for teaching medical students. From this clinical base the student is given the opportunity to see for himself the full meaning of social forces in health and disease. It is the responsibility of the teachers to exploit the advantages inherent in this setting. A number of recent reports describe the various ways[6, 8-13] in which the outpatient services are being developed for the training and education of undergraduate and graduate student.

There is increasing recognition in pediatric circles of the advantages of the outpatient department for teaching purposes, but there are suggestions that this recognition is more theoretical than real. In his presidential address, Levine[14] recognizes the need for "updating pediatric education" but fears that much of this is lip service. He goes on to say "The fact is that a Professor of Pediatrics is still reluctant to attend the outpatient clinic." In his review, "Pediatric Education Around the World". Wegman[15] summarized the deliberations of the IX International Congress of Pediatrics as follows: "It had been emphasized again and again that the outpatient department is the key place where pediatrics needs to be taught, that this is at the heart of good teaching. Here mother and child are seen together, here are seen the great majority of the problems which the physician will face in practice. If all in attendance at this meeting were questioned, many would say that they did not work in the outpatient department as much as in the wards. This was pointed out as a situation to be corrected, for if the professor or head of the department goes into the outpatient department, he will give it more status and others will come to realize the teaching potentiality there."

It is important that the teaching outpatient department serve a responsible medical role in the community and provide first-class medical care. There must be a suitable variety of undifferentiated and specialized clinical material to attract and stimulate the medical and paramedical staff.

As a participating member of an active medical unit the medical student can be placed in a position of limited responsibility with a family. He is motivated by a real life situation and becomes aware of and accepts responsibilities which were less meaningful in the lecture or ward round. He finds he has to familiarize himself with social resources in the community, to weigh the value of medical consultation, to assess whether a family can or cannot cope with a problem and what to do about it. He becomes aware of his own limitations, and of the limitations imposed upon him by the behaviour of his patients.

Teachers and students have long been aware of the hazards that arise when the hospitalized patient is the subject of a teaching round. While these same hazards apply to outpatient teaching, they are more likely to be offset by built-in controls (medical and paramedical staff and the mother). A child with his mother is viewed as a member of a family with an address and a home, and his disease is studied in relation to the social background. These are some of the intangible assets which the outpatient setting should exploit. This philosophy is well captured in the following quotation: "Above all, we would emphasize that it is the practical demonstration of medicine actually at work in an open society which is important. It is one thing to tell a student that there are no diseases but only sick persons; it is another thing to maneuver him into a doctor-patient relationship so that he can make this discovery for himself."[16]

During the past seven years the students in final-year medicine at the University of British Columbia have spent half of their five-week pediatric experience in the outpatient department.

On two or three mornings each week for 2½ hours the students conduct an office practice under the supervision of the medical staff. Each student has an appointment list of one new and two or

three "old" patients. After he has completed each case, the teaching supervisor discusses with him the findings, and appropriate investigations and management. The students are encouraged to attend with the child at any subsequent consultations and to discuss appropriate problems with the public health nurse or social worker. Problem cases are discussed for an hour at the beginning of the outpatient day and on two afternoons each week with the Medical Director. The presentation of an 18-month-old boy with 15 to 20 admissions to the emergency department for accidents, poison ingestion and so forth, and the ensuing discussions with the Children's Aid Society, serve to emphasize the role of social workers in the community. The discussion of a child with deafness and athetosis following hemolytic disease of the newborn, and the resultant family reactions, emphasize to the students the importance of early diagnosis of such defects and the value of comprehensive planning to modify them. They learn that factors other than medical pathology determine the course and the prognosis for these children.

On two or three afternoons the students are assigned to special clinics where they observe experienced physicians conducting consultation practice. In some situations the students carry out the basic examination and then discuss the condition with the clinician. In other clinics they are observers.

They have the customary experience in developing a diagnosis from the available evidence. The problems of management introduce them to the standard medical therapeutic weapons described by Scott, Anderson and Cartwright,[17] in their article "Just What the Doctor Ordered". In addition, they learn that medicine and sociology overlap in practice, and that part of effective medical care is the appropriate utilization of the community in the long-term management. The lack of such preparation for practice has recently been emphasized by Abrahams.[18]

It is readily apparent that there must be sufficient and senior physicians to supervise such a program. These physicians must know the community well and expertly involve social agencies without needlessly wasting their time. It is desirable to have pediatric staff drawn from the various types of practice, including private and consulting practice, and also full-time physicians from community agencies and institutions. Enlistment rather than conscription of the medical staff is more likely to ensure a group who enjoy teaching in the outpatient department. The supervisory job must not be a career step-ladder, or an appointment pending advancement elsewhere. Such a philosophy can too easily breed an environment which teaches how not to practise medicine.

As in all phases of education, the personal qualities of the teacher should provide a strong inspiring force. To exploit the advantages of the outpatient setting and thereby stimulate the students' interest and participation it is necessary to attract physicians with interest, ability and experience in this type of practice.

DISCUSSION

The past ten to fifteen years have witnessed an interesting evolution in outpatient departments in many hospitals, particularly those associated with medical schools. The changing pattern of mortality and morbidity in childhood has created an awareness of and interest in medical problems of a chronic nature with an intensification of efforts to detect and modify them. The effect of such illnesses upon the family and the effect of family strengths and weaknesses upon the care of these children have emphasized the need for comprehensive assessment and individualization of care based upon knowledge of family and community resources.

It is well recognized that government and voluntary societies have independently evolved diagnostic and therapeutic ambulatory resources for specific types of medical problems. On the other hand, in spite of the many programs, there are a number of children for whom no specific resource exists. Examples are children with multiple handicaps, with deafness and other communicative problems, with learning disabilities, or with autism or mental retardation. The outpatient department is ideally suited for the development of diagnostic resources for these more difficult problems. Thus, in addition to the traditional special clinics, the outpatient department has found it advisable to develop programs for complicated problems and for children with multiple handicaps. After outpatient assessment of the various problems and the order of their importance, the child can be referred to the most appropriate community resource, if such exists.

The advantages of an outpatient department in the study and evaluation of many children are becoming recognized. Experience shows that children with handicaps frequently have multiple problems, including medical, psychological and social difficulties or combinations of these. The child with cerebral palsy often has an intellectual or sensory deficit in addition to a motor handicap. The child with a post-rubella syndrome frequently has visual, auditory, cardiac and intellectual problems. This means that considerable diagnostic scope is essential in the primary evaluation of the child and the family, and the outpatient department with its available medical and paramedical staff with access to diagnostic facilities provides a unique centre for evaluation of such problems in children.

In view of the changing emphasis in child care and the development of community resources partly described above, the role of the physician has altered. In addition to the inpatient hospital role he is now a member and at times a leader of a team comprising many disciplines, including social work, public health nursing, teaching, psychology and so forth. Team work has its own hazards, however. The exposure to a variety of specialists

may lead to fragmentation of the child. Different consultants may offer conflicting opinions and thus create new anxieties for the family. The division of responsibility among the team members may lead to collective irresponsibility. Miller[19] has illustrated the need for an Ariadne figure to guide the patient through the maze of opinions. These hazards emphasize the need for an informed family counsellor to integrate and interpret the various studies.

Several recent studies of children in hospital[20-22] have emphasized that separation of child, particularly the preschool child, from his mother can be followed by important emotional sequelae. These reports have doubtless influenced current thinking concerning hospitalization of children, and have increased the demand for resources for ambulatory patients.

Paterson's[1] original concept deserves restatement: "To conclude therefore I would say that a health centre is not just a hospital outpatient department but it also embraces community services and public health services and these should be made available at all modern hospitals." It is apparent that the outpatient department of the Health Centre for Children has been highly developed as a consultative centre, in conjunction with the hospital and the medical school. Some integration with community services has also been achieved. This has been stimulated by the appointment of a public health nurse and social workers and some medical staff with training and experience in community methods of investigation and treatment.

The need to involve more workers of this kind has not been recognized everywhere. It is becoming increasingly urgent to bring the skills of the physicians in public service into the pediatric departments. The survival of many children with many formerly fatal genetic diseases poses new problems in society.[23] This common interest and responsibility demands a united effort to cope with the medical and social consequences. This is a new horizon for the preventive approach.

During the recent period of change in pediatric practice, pediatric education has assumed a greater importance. The scope of pediatric teaching has extended far beyond the traditional inpatient hospital work. Most pediatric departments have recognized the need to keep in step with the expansion of community health resources and some have offered leadership in their development.[24, 25]

The emphasis on outpatient teaching in medical education varies in different centres. The outpatient department of the Health Centre for Children is fortunate to possess a type of practice which offers exceptional opportunities for student teaching. On the one hand, an active consultative practice demonstrates to students the possibilities of investigation of ambulatory patients and the team approach. On the other hand, the day-to-day office practice of the medical clinic shows them aspects of medicine that demand a different type of investigation and therapy. This is a much coveted group of families for a teaching unit because the clinical situation involves consideration of the family problems which at times constitute such a burden for the physician in practice. These fundamentals of practice cannot be observed or taught in the wards or in the laboratories but can be demonstrated in the pediatric outpatient department from the waiting room onwards. Tonsils and stomach aches and rashes and headaches, bed wetting, discharging ears, fecal incontinence and speech problems—these are some of the troubles that bring children to the outpatient department. In the process of dealing with these, the student can be confronted with parental attitudes, mother-child relationships, cultural patterns, social maladjustment—the things that complicate and confound or resolve his daily work when later he enters practice.

This seems to us to be one way of enriching the student's education in pediatrics and of introducing him to his full responsibilities in child health.

SUMMARY

The evolution of the outpatient services at the Vancouver Health Centre for Children is described. The role of the outpatient department in the community and in medical education is discussed.

REFERENCES

1. PATERSON, D.: *Canad. M. A. J.*, **62**: 39, 1950.
2. World Health Organization: Report of Study Group on Pediatric Education, W.H.O. Technical Report Series No. 119, World Health Organization, Geneva, 1957.
3. MACLENNAN, J. M. AND SMALL, M. E.: *Lancet*, **1**: 142, 1955.
4. MOTT, G. A.: *Pub. Health*, **74**: 283, 1960.
5. PATERSON, D.: *Canad. M. A. J.*, **76**: 483, 1957.
6. SCOTT, R.: *J. M. Educ.*, **31**: 621, 1956.
7. RUMKE, H. C.: *In*: Proceedings of the First World Conference on Medical Education, held under the auspices of the World Medical Association, Oxford University Press, London, 1954, p. 660.
8. WHITE, K. L.: *Canad. M. A. J.*, **80**: 506, 1959.
9. GREGG, L. A. AND MOSES, C.: *J. M. Educ.*, **31**: 757, 1956.
10. KORSCH, B. M. AND LEVINE, S. Z.: *Pediatrics*, **14**: 171, 1954.
11. PARMELEE, A. H., JR., SWENGEL, E. AND ADAMS, J. M.: *Ibid.*, **14**: 387, 1954.
12. SOLNIT, A. J. AND SENN, M. J. E.: *Ibid.*, **14**: 547, 1954.
13. COLMORE, J. P. AND WOLF, S.: *J. A. M. A.*, **156**: 830, 1954.
14. LEVINE, S. Z.: *A.M.A. Am. J. Dis. Child.*, **100**: 651, 1960.
15. WEGMAN, M. E.: *J. M. Educ.*, **36**: 38, 1961.
16. SCOTT, R.: *Brit. M. J.*, **2**: 577, 1958.
17. SCOTT, R., ANDERSON, J. A. D. AND CARTWRIGHT, A.: *Ibid.*, **2**: 293, 1960.
18. ABRAHAMS, S. I.: *Pub. Health*, **75**: 90, 1961.
19. MILLER, C. A.: Health needs of children with multiple handicaps, *In*: Institute on the Prevention and Management of Handicapping Conditions in Infancy and Childhood, University of Michigan, November 16-20, 1959, University of Michigan, Continued Education Service, Ann Arbor, Mich., 1960.
20. VAUGHAN, G. F.: *Lancet*, **1**: 1117, 1957.
21. BOWLBY, J.: Maternal care and maternal health, World Health Organization Monograph Series No. 2, World Health Organization, Geneva, 1951.
22. PRUGH, D. G. *et al.*: *Am. J. Orthopsychiat.*, **23**: 70, 1953.
23. WRIGHT, S.: On the appraisal of genetic effects of radiation in man, *In*: A Report to the Public on Biological Effects of Atomic Radiation, based on the 1960 summary reports of the National Academy of Sciences Committee on the Biological Effects of Atomic Radiation, National Academy of Sciences, Washington, D.C., 1960, p. 18.
24. DEISHER, R. W.: *Pediatrics*, **16**: 541, 1955.
25. *Idem*: *Ibid.*, **11**: 538, 1953.

Canad. M. A. J.
July 22, 1961, vol. 85

CASE REPORT

TRIMETHADIONE HEPATITIS
A CASE REPORT AND REVIEW OF TRIMETHADIONE TOXICITY

J. L. LEBLANC, M.D. and
A. FELDMAN, M.D., *Montreal*

A GREAT DEAL has been written about the toxic effects of trimethadione or 3,5,5-trimethyl-2,4, oxazolidinedione (Tridione). Trimethadione hepatitis, however, has been encountered only rarely.

REVIEW OF TRIMETHADIONE TOXICITY

Spielman, in 1944, first synthesized trimethadione, reporting the drug to have "the analgesic potency of ASA" and to have "a remarkably low toxicity". Richards and Everett,[1] a few months later, reported that in experimental animals it has a markedly antagonistic effect against the convulsant action of pentylene tetrazol (Metrazol), picrotoxin and electroshock but not of strychnine. The next year, Goodman and Gilman[2] reported that in animals residual anticonvulsant action from single doses could be noted up to 48 hours. Since that time, many toxic reactions have been attributed to this drug, but only once before has mention been made of hepatic dysfunction (Leard, Greer and Kaufman).[3]

Lennox[4] in 1945 reported the first toxic manifestation, namely, unusual sensitivity of the eyes to bright sunlight. In a later report[5] on the use of the drug in 222 patients, a number of instances of several toxic manifestations were noted: photophobia in 122; rash, either acneiform or morbilliform, in 32; gastric distress or nausea in 18; behaviour difficulty in 9; headache in 7; insomnia, poor appetite and nervousness in 4; dizziness, pain in eyes and nosebleeds in 3; sleepiness, double vision and poor circulation in 2; and sneezing, hiccuping and aplastic anemia in 1.

A complete hematological report on these cases was made by Davis and Lennox in 1947.[6]

Six per cent of 127 patients demonstrated a decrease in the polymorphonuclear leukocyte count and 25% showed an eosinophilia.

At this time, the side effects were considered to be minimal as compared to the benefits in the treatment of petit mal epilepsy, and the medication was given without undue concern.

It was only in May 1948 that serious toxic manifestations of the drug came to light. It was at this time that Barnett, Simons and Wells[7] described, for the first time, the appearance of nephrotic syndrome in a patient receiving trimethadione. Their patient, a girl of 16 years, developed edema, an increased serum cholesterol level and a decreased serum albumin level on two different occasions while on trimethadione therapy. Several months after the withdrawal of the medication the biochemical results returned to normal.

Since that time many others have recorded similar cases: White,[8] Nabarro and Rosenheim,[9] Barnett, Forman and Lauson,[10] Rosenblum, Sonnenschein and Minsky[11] and others.

Aplastic anemia and agranulocytosis are also common toxic manifestations of trimethadione therapy. In 1946, one of the first cases of aplastic anemia was reported by Mackay and Gottstein.[12] Carnicelli and Tedeschi,[13] Braithwaite,[14] Briggs and Emery,[15] and Gentry and Hill[16] described similar cases.

Leard, Greer and Kaufman[3] described a case of "hepatitis", exfoliative dermatitis and leukemoid reaction in bone marrow in a 69-year-old white male during trimethadione therapy; the patient recovered.

An 8-year-old white boy was first seen in September 1959 for spells during which he would "stop and stare as if in a daze". A clinical diagnosis of petit mal was confirmed by electroencephalography. No family history of epilepsy could be elicited. On October 5, 1959, the patient was started on trimethadione, 150 mg. four times daily, and phenobarbital 15 mg. four times daily.

Two weeks after the start of treatment the patient was seen because of a generalized rash (an erythematous papular rash over the entire body) and an elevated temperature. His condition was followed over a three-day period while he remained at home. He was then admitted to hospital and given triamcinolone therapy; all antiepileptic medications were discontinued. At the time of discharge three days later the rash had completely faded and he was sent home without medication.

Four days after his first admission the patient developed a typical erythema multiforme rash and a temperature of 106° F. Four days later jaundice appeared and he was hospitalized once again.

On physical examination he was toxic, irrational, restless and jaundiced. His temperature was 99° F. A tender liver was palpable two fingerbreadths below the right costal margin. Herpetic-type lesions were found on the soft palate. An intravenous infusion of glucose and water was started, the only "medication" given.

It was felt that this child manifested extreme sensitivity to trimethadione and that the onset of this illness had been temporarily arrested by the use of steroid therapy on his first admission.

The eruption gradually faded, desquamation following. The vesicular mucous membrane lesions healed spontaneously.

Laboratory findings.—The urine contained +++ bile, but was otherwise negative. The hemoglobin value was 12.5 g. %. The white blood cell count was 8613, with 4611 polymorphonuclear leukocytes, 435 eosino-

phils, 87 basophils, 3045 lymphocytes and 435 monocytes.

On November 2, the total bilirubin level was 5.4 mg. %, direct 3.45 mg. %; thymol turbidity, 2.3; and cephalin cholesterol flocculation, 0.

On November 9, the total bilirubin level was 7.35 mg. %, direct, 6.45 mg. %; thymol turbidity, 2.9; and cephalin cholesterol flocculation, 4+.

The Paul-Bunnell test was negative.

The subsequent course of the illness was uneventful, the liver decreasing in size and the liver function tests showing improvement.

It is of interest that an electroencephalogram taken in December 1959 showed marked improvement with disappearance of the classical petit mal pattern.

DISCUSSION

Trimethadione is an excellent medication for the treatment of the petit mal triad of episodes of absence, akinesis and myoclonic jerks[17-26] occurring singly or together in a patient with characteristic 3/sec. spike and wave discharges, bilaterally symmetrically and most prominent anteriorly on the electroencephalogram.

However, it must be remembered that trimethadione is a potentially toxic agent to the skin, bone marrow, kidneys and, as now demonstrated, to the liver.

It is possible that in the case presented the reactions were on an allergic basis rather than due to direct organ toxicity. It is probable that if trimethadione had a direct hepatotoxic action this would have become evident in animal experiments, and cases of human toxic hepatitis would be much more frequent.

Toxic reactions appear to be related to extreme sensitivity or idiosyncrasy rather than to overdosage. No correlation has been noted between dose, duration of dose, age or sex in the fatalities reported.[26]

Frequent peripheral blood assessment, urinalysis and careful clinical observation during trimethadione therapy still are the most effective measures to be taken in our present state of knowledge during treatment of petit mal.

Davis and Lennox[6] further suggest that the drug not be given to patients who have a history of blood dyscrasia or a pronounced idiosyncrasy to drugs. Although no relation between such a background and the occurrence of reactions to trimethadione has been shown, this rule is probably a good one to follow for greater safety.

SUMMARY

Trimethadione toxicity is reviewed. The case of an 8-year-old boy treated for petit mal epilepsy by trimethadione who developed fever, erythema multiforme and hepatitis is reported. Hepatitis is a rarely recognized toxic reaction to this drug.

REFERENCES

1. RICHARDS, R. K. AND EVERETT, G. M.: *Fed. Proc.*, **3**: 39, 1944 (abstract).
2. GOODMAN, L. S. AND GILMAN, A.: Pharmacological bases of therapeutics, The Macmillan Company, New York, 1955, p. 192.
3. LEARD, S. E., GREER, W. E. R. AND KAUFMAN, I. C.: *New England J. Med.*, **240**: 962, 1949.
4. LENNOX, W. G.: *J. A. M. A.*, **129**: 1069, 1945.
5. *Idem*: *Ibid.*, **134**: 138, 1947.
6. DAVIS, J. P. AND LENNOX, W. G.: *J. Pediat.*, **31**: 24, 1947.
7. BARNETT, H. L., SIMONS, D. J. AND WELLS, R. E.: *Am. J. Med.*, **4**: 760, 1948.
8. WHITE, J. C.: *J. A. M. A.*, **139**: 376, 1949.
9. NABARRO, J. D. N. AND ROSENHEIM, M. L.: *Lancet*, **1**: 1091, 1952.
10. BARNETT, H. L., FORMAN, C. W. AND LAUSON, H. D.: *Advance. Pediat.*, **5**: 53, 1952.
11. ROSENBLUM, J., SONNENSCHEIN, H. AND MINSKY, A.: *A.M.A. J. Dis. Child.*, **97**: 790, 1959.
12. MACKAY, R. P. AND GOTTSTEIN, W. K.: *J. A. M. A.*, **132**: 13, 1946; correction, **132**: 163, 1946.
13. CARNICELLI, T. J. AND TEDESCHI, C. G.: *New England J. Med.*, **238**: 314, 1948.
14. BRAITHWAITE, R. F.: *Brit. M. J.*, **1**: 14, 1948.
15. BRIGGS, J. N. AND EMERY, J. L.: *Lancet*, **1**: 59, 1949.
16. GENTRY, E. F. AND HILL, L. F.: *Am. J. Dis. Child.*, **75**: 582, 1948.
17. THORNE, F. C.: *Psychiat. Quart.*, **19**: 686, 1945.
18. PERLSTEIN, M. A. AND ANDELMAN, M. B.: *J. Pediat.*, **29**: 20, 1946.
19. BICKEL, M. G.: *Rev. méd. Suisse Rom.*, **67**: 267, 1947.
20. WHITTY, C. W. M.: *Brit. M. J.*, **2**: 311, 1949.
21. DAVIES, G. R. AND SPILLANE, J. D.: *Brain*, **72**: 140, 1949.
22. Annotation: *Lancet*, **1**: 221, 1948.
23. KAPLAN, M., MOZZICONACCI, P. AND NEKHOROCHEFF, I.: *Semaine hôp. Paris*, **25**: 365, 1949.
24. FORSEY, R. R. AND BLACK, R. W.: *Canad. M. A. J.*, **64**: 120, 1951.
25. LIVINGSTON, S. AND BOKS, L. L.: *New England J. Med.*, **253**: 138, 1955.
26. WELLS, C. E.: *A.M.A. Arch. Neurol. & Psychiat.*, **77**: 140, 1957.

5778 Smart Avenue,
Town of Côte St. Luc, Que.

PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

The annual commencement of the University of Toronto was held in Convocation Hall June 9th, 1911. The degree of LL.D. was conferred *honoris causa* upon the Right Honourable Sir Charles Fitzpatrick, who was presented by the Chief Justice of Ontario, and upon Elgin R. L. Gould, B.A., Ph.D., of New York, presented by the president of Victoria College. The Dean of the faculty of medicine presented Dr. Wilfred Grenfell for the honorary degree of Doctor of Medicine, which was granted amid a hearty display of enthusiasm by the large audience. A Diploma of Public Health was given Dr. Hibbert Winston Hill, of the Health Department of the State of Minnesota. He was presented by Dr. William Oldright. A total of 752 degrees was conferred upon graduates in various faculties and departments. In the faculty of medicine 143 were admitted as Bachelors of Medicine. Twenty-one of these were graduates in Arts, and five of the total number were women. The gold medal was awarded to J. M. Livingstone; the first silver medal to A. S. Eagles; the second silver medal to C. Bouck and N. A. Christie, and the third silver medal to J. G. A. Campbell. The Chappell prize in clinical medicine was won by H. W. Benson, and for the George Brown Memorial Scholarship in medical science, J. M. Livingstone, L. A. Roy, L. O. C. Skeeles, and J. G. A. Campbell ranked in the order named.—*Canad. M. A. J.*, 1: 688, 1911.

Canad. M. A. J.
July 22, 1961, vol. 85

SHORT COMMUNICATION

HEXAMETHONIUM IN THE TREATMENT OF ACUTE PULMONARY EDEMA

A. W. PERRY, M.D., F.R.C.P.[C], *Victoria, B.C.*

IN 1952 THE effect of ganglionic blockade in acute pulmonary edema was demonstrated.[1] In 1956 Ellestad and Olson[2] reported on the treatment of 19 cases of acute pulmonary edema by hexamethonium. Twelve of the patients so treated showed an excellent response and four a good response. Despite these reports the value of hexamethonium seems to have been little appreciated and, indeed, there is now difficulty in obtaining this drug. It was therefore felt worth while to report further experience in the use of hexamethonium in the treatment of acute pulmonary edema.

CASE 1.—A 30-year-old man was admitted to the Royal Jubilee Hospital, Victoria, B.C., on March 13, 1958, for drainage of an abscess which had developed at the site of an open reduction of a fractured right clavicle. Drainage was performed on the day of admission. The next day the patient developed a reddened, tender area over the extensor surface of the left forearm. He was given erythromycin but the area gradually became more swollen and fluctuant. On March 21, 1958, the area was incised and a copious yellow discharge was obtained. During the next two days he became acutely ill with fever and chills, left pleuritic pain and left flank pain. Intramuscular chloramphenicol (Chloromycetin) was added to his therapy.

When seen on March 23, 1958, he appeared acutely ill. He was flushed and perspiring and had a rapid, bounding pulse. There were draining abscesses over the right clavicle and left forearm and an area of induration over the left shin. Petechiae were seen on the hands. In the left lower chest breath sounds were decreased and there were scattered rales. The heart was not enlarged to percussion. There was a grade one blowing systolic aortic murmur. The blood pressure was 150/90 mm. Hg. The clinical picture was that of a septicemia with possible endocarditis and a left lower lobe pneumonia. *Staphylococcus aureus* had been cultured from the areas drained. Over the next four days treatment consisted of administration of chloramphenicol, 1 g. intramuscularly every six hours; erythromycin, 500 mg. every six hours by mouth; penicillin, 10 million units intramuscularly in divided doses; gamma globulin, 3 c.c. intramuscularly every eight hours; and staphylococcus antitoxin, 10,000 units intramuscularly every 12 hours.

After transitory improvement the patient became more ill and very toxic in appearance. The antitoxin dosage was increased to 10,000 units every six hours and spiramycine (Rovamycine) 1.25 g. was given by mouth every six hours in addition to the other antibiotics. On March 29 chloramphenicol and penicillin were discontinued and ristocetin, 1 g. in 250 c.c. of 5% glucose in water, was administered every eight hours. That day, however, breathlessness became evident and the patient developed a gallop rhythm with a pulse of 144 per minute. Sodium intake was restricted and over the next 24 hours he was given digoxin 0.75 mg. intravenously and 1 mg. by mouth. On the following two days digoxin, 0.25 mg., was given daily but late on the evening of the second day the patient developed severe pulmonary edema. He had been given morphine ¼ grain intramuscularly just before he was seen. At this time he appeared moribund: his colour was a mottled greyish blue and bloody froth was dripping from his mouth. He was unconscious and his eyes were rolled up. The heart sounds were obscured by rales and rhonchi. His blood pressure was 230/100 mm. Hg and his pulse was 140 per minute and regular. Oxygen was given by B.L.B. mask at 10 litres per minute and 400 c.c. of blood was removed by venesection. He was placed in a sitting position. No improvement occurred and it appeared that he was about to expire. Hexamethonium was then administered intravenously in a dose of 2.5 mg. measured in a tuberculin syringe (0.1 c.c. of a 25 mg./c.c. preparation, diluted to 1 c.c. with normal saline and given over a period of two minutes). Since some of the fluid escaped about the hub of the needle, a second dose of 2.5 mg. was given. The response was immediate. His breathing became less laboured and within two to three minutes he had regained consciousness. Within 10 minutes he was breathing quite normally and his chest was clear to auscultation. The subsequent course in hospital was one of gradual improvement and he was discharged well on May 14, 1958.

COMMENT

This case demonstrated the life-saving potential of hexamethonium. This patient's pulmonary edema was likely due to a fluid overload superimposed upon cardiovascular damage by the staphylococcal toxemia and possibly by a staphylococcal endocarditis. This first experience with the use of hexamethonium for acute pulmonary edema was quite impressive.

CASE 2.—An 82-year-old man was seen in the emergency department of the Royal Jubilee Hospital on the evening of June 26, 1959, because of acute dyspnea. He had known heart disease and had been taking digoxin 0.25 mg. daily. He was initially given a further 0.5 mg. digoxin intravenously, aminophylline grains 7½ intravenously and morphine grain ⅜ intravenously. Rotating tourniquets and oxygen were used and he was placed in a sitting position in a chair. His condition did not improve and when seen by the author shortly after the above treatment he was semi-comatose and cyanosed, and had wheezing bubbling respirations. The pulse was 120 per minute and regular. His blood pressure was 220/130 mm. Hg. Hexamethonium 2.5 mg. diluted to 1.0 c.c. with saline was given intravenously over a period of about two to three minutes. Over the next 10 minutes the blood pressure fell to 110/70 and the patient became fully responsive. The chest became clear, except for basal rales. His further

course in hospital was uneventful with treatment consisting of digitalis, sodium restriction and diuretics.

COMMENT

This case demonstrated the value of hexamethonium in acute pulmonary edema refractory to other modes of treatment.

CASE 3.—This 75-year-old man was seen at 3:00 a.m. on March 23, 1960, at the Royal Jubilee Hospital, because of severe dyspnea. No history was obtainable other than that he had been treated for heart disease; it was not known whether this had included digitalis. He had awakened with shortness of breath which had become progressively worse. On examination, he was a frail, elderly man, of grey colour, perspiring profusely and with white froth dripping from his mouth. The neck veins were distended. The heart sounds could not be heard because of coarse, bubbling rales, present throughout the chest. The pulse was 120 per minute and regular. His blood pressure varied from 130 to 150 mm. Hg systolic and 90 to 120 diastolic. There was slight ankle edema. Oxygen was given and the patient was lifted into a chair. Despite the degree of pulmonary edema the patient had feeble respirations and it was decided not to give him morphine. Hexamethonium, 2.5 mg. in 1 c.c. of saline, was given intravenously over a two-minute period. At the end of this time the blood pressure had fallen to 110 to 120 systolic, over 70 to 80 diastolic, and within five minutes the patient's chest had almost cleared; one could then hear the loud murmur of aortic stenosis. Subsequently it was ascertained that the patient had not been taking his digitalis and his cardiac failure was controlled with digitalis and sodium restriction.

COMMENT

This case demonstrates the usefulness of hexamethonium in a patient with pulmonary edema when it is not known whether digitalis has been used or not, with a resulting reluctance to risk giving digitalis.

CASE 4.—On February 11, 1961, a 71-year-old woman was admitted to the Royal Jubilee Hospital because of shortness of breath. She had had dyspnea on exertion for six weeks and occasionally had had nocturnal dyspnea. She had not consulted her physician and had had no treatment. She was awakened just prior to admission by severe dyspnea. There was no history of chest pain and no known previous heart disease. When seen shortly after admission she presented the picture of acute pulmonary edema. She was pale and perspiring freely. There was audible expiratory wheezing, the pulse was 130 per minute and regular, and the blood pressure was 174/140 mm. Hg. The apex was percussed two fingerbreadths beyond the midclavicular line, but the heart sounds could not be heard because of rales, rhonchi and wheezing throughout the chest. In view of the previous experiences it was thought to be of interest to see how much improvement would follow the administration of hexamethonium to a patient who had had no other treatment. Hexamethonium, 2.5 mg., was given intravenously, following the same technique as described in the previous cases. Within three minutes the blood pressure fell to 135/80 mm. Hg and the wheezing pretty well disappeared, but rales in the chest persisted. In seven minutes the pulse rate was 112 per minute and the blood pressure 140/84; the patient felt quite relieved and on examination there was no longer any wheezing, the coarse rales had cleared and there were only fine rales at the lung bases.

COMMENT

This patient demonstrates that hexamethonium may be of use in acute pulmonary edema even though other treatment has not been given.

CONCLUSION

In addition to the cases cited above, hexamethonium was used on a number of occasions in treating patients with renal failure who had become overhydrated and had developed pulmonary edema. Such patients were seen on several occasions prior to the employment of dialysis by the artificial kidney. The hexamethonium has proved of great value in tiding these patients over until dialysis was effective in eliminating the excess fluid.

This experience with hexamethonium is in accordance with that described by others. It is felt that hexamethonium should hold an important place in the treatment of acute pulmonary edema.

316 Yarrow Building,
Victoria, B.C.

REFERENCES

1. SARNOFF, S. J., GOODALE, W. T. AND SARNOFF, L. C.: *Circulation*, **6**: 63, 1952.
2. ELLESTAD, M. H. AND OLSON, W. H.: *J. A. M. A.*, **161**: 49, 1956.

PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

ONTARIO MEDICAL ASSOCIATION

The meeting of the Ontario Medical Association, which was held at Niagara Falls, was the thirtieth in the history of that important organization. There were present two hundred and fifty members and fifty visitors, and this large registration alone attests the importance of the association. Every division of medicine was represented in the sections upon medicine, surgery, preventive medicine and military hygiene, obstetrics and gynaecology, and ear, eye, nose, and throat. The meeting lasted three days and five sessions were held. An important feature of the meeting was the address by Dr. Russell Park, of Buffalo, upon "The History of Medicine in America".

The officers elected for 1911-12 are: president, Dr. H. A. Bruce, Toronto; first vice-president, Dr. F. W. E. Wilson, Niagara Falls; second vice-president, Dr. Wm. Hall, Brantford; third vice-president, Dr. F. P. Drake, London; fourth vice-president, Dr. George Field, Cobourg; treasurer, Dr. J. Heurner Mullin, Hamilton; general secretary, Dr. F. Arnold Clarkson, 471 College Street, Toronto. Upon the strength of the provincial association depends the strength of the Canadian Medical Association, since all are bound up in a common cause.—*Canad. M. A. J.*, 1: 679, 1911.

Canad. M. A. J.
July 22, 1961, vol. 85

THE CANADIAN MEDICAL ASSOCIATION
JOURNAL
LE JOURNAL DE
L'ASSOCIATION MÉDICALE CANADIENNE

published weekly by
THE CANADIAN MEDICAL ASSOCIATION
Editor, C.M.A. Publications:
DONALD C. GRAHAM, M.D., F.R.C.P.[C]
Managing Editor: T. C. ROUTLEY, M.D., F.R.C.P.[C]
Associate Editors:
GORDON T. DICKINSON, M.D.
JOHN O. GODDEN, M.D., M.S.(Med.)
Assistant to the Editor: ROBERT L. RANDALL

Editorial Offices: 150 ST. GEORGE ST., TORONTO
(Information regarding contributions and advertising will be found on the second page following the reading material.)

GROUND RULES FOR STUDIES IN CARCINOGENESIS

CURRENTLY, in some fields of cancer research, emphasis has shifted away from attempts to develop "curative" therapy, and is being directed instead toward preventive measures. Prevention requires either the removal of carcinogenic hazards from the environment or the correction of deficiencies which favour cancer induction. Specific deficiencies, such as that of iron associated, in the Plummer-Vinson syndrome, with carcinoma of the esophagus, are rare, so that means of *changing the environment of people who have not yet developed cancer* are needed to supplement current, and future, therapeutic measures.

In a recent issue of the *Nova Scotia Medical Bulletin* (5: 134, 1961), F. J. C. Roe, Pathologist to the Cancer Research Department of the London Hospital Medical College, has reviewed the role of animal experiments in the detection and evaluation of cancer hazards in our environment, in order to establish a basis upon which the validity of animal tests can be judged. His review, which will appeal to any physician interested in a broader view of cancer control, is distinguished by its avoidance of jargon, reasonable tone, sturdy common sense and the absence of special pleading.

The value of animal studies in detecting human cancer hazards is now well established. Epidemiological studies that reveal correlations of high probability are still of fundamental importance despite the views of a minority who argue, for example, that the high incidence of cancer of the nose and bronchus in nickel workers *just as likely* is due to the fact that men who are peculiar, in wanting to work in the nickel industry, are also peculiar in having a high expectation of developing nose and lung cancer. However, prospective statistical studies, from which the best data in this field come, are expensive and may not always be practicable if: (a) a long latent period exists between exposure and tumour induction; (b) the overall incidence of the particular human cancer is very low; and (c) the control of other possibly relevant environmental differences is difficult. When statistical studies cannot provide a clear-cut answer, the possibilities of direct approach are exhausted, for substances cannot be tested *deliberately* for their carcinogenic action on man. Here, as in almost every other branch of medical research, tests on *other* animal species are necessary.

Even when satisfactory statistical tests in man are practicable, carefully selected animal tests can provide certain answers much more quickly. In the dye-stuff industry, for example, where workers were exposed to benzidine or to naphthylamine, between 15 and 25 years usually elapsed from the beginning of exposure to the time when the first cases of bladder cancer were seen. The average induction-time, in relation to a particular form and rate of exposure, was approximately one-quarter to one-third of the average life span. By treating mice with the same substance, a high incidence of bladder tumours can be produced in approximately the same proportion of the exposed subjects' life span, i.e., 25 to 40 weeks.

Though it is desirable to define the general principles of design for such animal studies, there can be no inflexible standardized test regimen. The precautions necessary in the interpretation of experimental results are many, and involve, among other factors, the purity of the substance under test, the uses (and abuses) of tests of statistical significance, the peculiarities of species and test tissues, the criteria of malignancy ("the truth is that there is no clear-cut distinction between benign and malignant"), the significance of the induction of benign tumours, and confirmation by the repetition of the experiment.

In discussing the extrapolation of the results of animal experiments to man, Dr. Roe presents the core of his contribution. A positive result obtained in animals gains increasing significance for man if: (a) cancer is induced in more than one tissue and species, and by a dose and exposure appropriate to the carcinogen under study; (b) cancer is induced in the same tissue and is of the same histological type as that which the agent is suspected of inducing in man; (c) a retrospective statistical study in man shows a significant association. None of these types of evidence, however, constitutes absolute proof of a cause-and-effect relationship, and action can only be taken in the light of evidence based on the balance of probabilities.

When a substance which is considered hazardous can be eliminated from the environment without serious economic loss or interference with established practice, it should be done as soon as legislative inertia can be overcome. (It took the late Chevalier Jackson almost 20 years to persuade the New York State legislature to put poison labels on lye cans.) There can be no serious disagreement

here. In other cases, because of lack of alternatives, because possible alternatives carry their own hazards, or for serious economic reasons, it may be necessary to compromise by agreeing to *permissible levels* of exposure. This is an interim solution only, and complete elimination of the carcinogen should be the goal.

Every attempt should be made to prevent the further addition of hazardous factors to the environment, but still more attention must be paid to the evaluation and elimination of existing hazards. The agent 3,4-benzpyrene, a ubiquitous carcinogenic substance of considerable potency, has been demonstrated in "polluted" air, in cigarette smoke, in automobile exhausts, in smoked foods and in coffee grounds and can be produced by the pyrolysis or burning of almost any organic material. The existence of substances of this kind in almost every compartment of man's environment presents a very complicated problem of assessment and their elimination an enormous challenge to research workers in many fields, especially that of engineering.

It is a pity that this thoughtful exploration of a complex and highly important subject will not have wider circulation, though the Editors of the *Nova Scotia Medical Bulletin* are to be congratulated on their perspicacity in obtaining such a useful contribution to current medical literature.

AUTOPSY ON A MURDER TRIAL

THE British are one of the world's more law-abiding peoples, in whose well-governed islands murder has been gratifyingly infrequent for at least a century. Every year about 150 to 200 murders have been "known to the police", as the phrase goes, during this period. The numbers have fluctuated only a little in spite of increases in population, social change, political upheaval and great wars, yet the casual reader of the British press would seldom suspect that murder was so infrequent—only between two and three cases per million of population—for there are few people so keen as the British on reading about mayhem. It is difficult to grasp why so much is written, and often very well written, about so very few murders. British murders have their special style, and even when they are of the charnel-house type, like the series committed at 10 Rillington Place, Notting Hill, London, they are permeated by a certain sedate and sordid coziness.

Before the fatal act the murderer and his victim often take a nice cup of tea together, and once it has been committed the survivor enjoys further refreshment of this sort before disposing of the body. Even Scotland Yard may halt in the middle of its deliberations, or suspend an interrogation, for that cup of tea. There is a ceremonious formality about the whole business. Detective story writers seek to evoke this leisurely but sinister atmosphere, and for the aficionado of the sport there can be few better ways of relaxing after a day spent in coping with the mysteries of medical practice than one of these intelligent whodunits.

A recently published book by Ludovic Kennedy[1] has all the qualities of the best type of British murder story, but it happens to be perfectly true. It grips one because any one of us could find himself involved in another 10 Rillington Place, in some capacity or other. The bare bones of the story is that in 1950 an illiterate Welsh lad called Timothy Evans was hanged for strangling his infant daughter, Geraldine, and by inference, his wife Beryl too. The evidence which convicted him came largely from a man called Christie. Christie was a veteran of World War I, a man of considerable intelligence, who had in addition been a policeman for some years. Evans claimed that Christie had killed his wife, and supposed that he had killed the little girl too. But Evans was a high-grade mental defective, and also a bit of a liar.

From the start the police seemed to have believed Christie rather than Evans, for Christie being an ex-policeman knew exactly what to say, and what perhaps was just as important, what not to say. Evans went to his death protesting his innocence. Christie was not too well during the trial, but he managed to give evidence and his ailing condition gained him sympathy rather than suspicion. Mrs. Christie, too, supported her husband's evidence. It seems that he was a persuasive man, but one wonders whether even his persuasiveness would have managed to keep the police off the track had they noticed an old femur lying about in the yard, and discovered the skull that was in the bottom of his trash can during their first visit to 10 Rillington Place. These were relics of earlier essays in murder and necrophily which luckily for Christie went unnoticed. In December 1952 he murdered his faithful wife and buried her under the floorboards of the front room. Between then and his arrest on April Fool's Day 1953 he killed and stored away in his house three prostitutes. They were tied up neatly in blankets and stacked in a cupboard. His technique does not seem to have varied much. He first gassed his victims, then strangled them with a little rope which he kept for the purpose, and finally had necrophilous intercourse just after death. In March 1953 he sublet his suite, but after a few days the new tenants discovered that they were sharing their house and garden with the remains of no fewer than six women. The information that there were now six more corpses to be accounted for at 10 Rillington Place can hardly have been welcome to the authorities, particularly since the Lord Chancellor, Lord Kilmuir, had stated some years before that there was no practical possibility of an innocent man being hanged in that country, and that anyone who thought there was, was moving in the realms of fantasy. This was of course one of those dangerous statements that public men make so easily, for everyone knows that fact is

Canad. M. A. J.
July 22, 1961, vol. 85

regularly less credible than fantasy. Rather awkwardly too, Christie confessed that he had killed Evan's wife but he was not quite sure about the baby. It was embarrassing.

The trial made very clear that Christie was a pathological killer who had killed twice in 1943-1944, had presumably killed Mrs. Evans and her baby in 1949, and then had had another outburst of killing in 1952 and early 1953. Christie's own account suggested that he killed either to put people out of their misery, or because loose women forced themselves upon him, and indeed he was a very respectable man, at least on the surface. The British Government were urged vigorously to look into the curious coincidence by which 10 Rillington Place appeared to have housed two stranglers simultaneously. Accordingly the Lord Chancellor appointed a Mr. Scott Henderson, Q.C., as a one-man commission to make a brisk enquiry into the Evans-Christie affair. Christie himself was now due to be hanged, so there was some urgency. Mr. Scott Henderson's report was reassuring; all was well, and Evans had been hanged justly. Since Christie too followed him to the gallows it would seem that everything had been neatly tidied up, but as Mr. Kennedy's fascinating book shows, it has not turned out that way at all.

From the very start there was some evidence that Mrs. Evans had been a victim of one of Christie's necrophilous assaults. Although Dr. Teare, the very experienced police pathologist, reported his findings, they were never followed up. Indeed they were ignored by prosecution and defence alike. This oversight becomes more understandable when it is recalled that at this time no one knew of the two corpses in the garden: and even a femur leaning against the fence passed unnoticed. It is a classic example of "set".

At the very start the police decided that the dull-witted and untruthful Timothy Evans was their man. From that point Christie could not be seen as a suspect. He became a valuable ally, indeed an essential witness. It was true that he had spent a few years in prison as a young man, but in the interval he had been a policeman, had taken first-aid courses, and had, it is said, been well recommended. It appeared incredible and also unsporting to suggest that a well-respected man like Christie could have killed Mrs. Evans and the baby. But would it have seemed either unsporting or incredible had the police spotted that femur? Medical postmortem findings are often disillusioning for the diagnostician, but they have also been educative. Indeed, modern clinical medicine was built by relating clinical to autopsy findings. One extreme proponent of this valuable method was wont to urge, in his lectures in medical pathology, that every patient should be followed from the sick bed to the morgue, an ambition which excluded any hope of recovery. It seems that particularly in capital cases there is an immense reluctance on the part of the official law to admit even the possibility of error. The unwillingness to accept such a possibility is enhanced where error involves the execution of a supposedly guilty person. Lawyers, generally speaking, are wedded to a belief that their processes, hallowed by tradition, must work. Perhaps they usually do, but a reading of Mr. Kennedy's book will make the most complacent feel at least some uneasiness. This book should surely be obligatory reading for coroners, forensic pathologists, and psychiatrists, in whose province it lies especially, but it is also good reading for any medical man who enjoys a well-flavoured, seedy, London detective story which is also true. It raises a number of fascinating medicolegal points. Perhaps the most urgent of these is whether we are yet so infallibly correct at deciding who is lying and who is not that we should stake anyone's life on it: even the life of a feckless, untruthful and half-witted young man like Timothy Evans.

H.O.

REFERENCE

1. KENNEDY, L.: Ten Rillington Place, Victor Gollancz, London, 1961.

PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

Oliver Wendell Holmes reminds us that "medicine, sometimes impertinently, often ignorantly, often carelessly, called 'allopathy,' appropriates everything from every source that can be of the slightest use to anybody who is ailing in any way, or like to be ailing from any cause. It learned from a monk how to use antimony, from a Jesuit how to cure agues, from a friar how to cut for stone, from a soldier how to treat gout, from a sailor how to keep off scurvy, from a port-master how to sound the eustachian tube, from a dairy-maid how to prevent small-pox, and from an old market woman how to catch the itch insect. It borrowed acupuncture from the Japanese heathen, and was taught the use of lobelia by the American savage." Though such a statement is true, we must remember that the men who culled scientific truth from such unlikely sources were, for the most part, fitted by special training for the work they accomplished so well. Thus, Edward Jenner was a pupil under John Hunter, and had become "an expert anatomist, a sound pathologist, a careful experimenter, and a good naturalist"; a period of thirty years was spent in research before he announced to the world the discovery of vaccination. Even the friar who cut for stone attained his skill after many courses of dissection and experiments on the dead.—A. Primrose: 1911 Address in Surgery to the Canadian Medical Association, *Canad. M. A. J.*, 1: 615, 1961.

Letters to the Journal

ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF CANADA: STATEMENT CONCERNING DICHOTOMY OF FEES AND PRINCIPLES OF FINANCIAL RELATIONS IN THE PROFESSIONAL CARE OF THE PATIENT

To the Editor:

The statement by the Royal College of Physicians and Surgeons on the dichotomy of fees (*Canad. M. A. J.*, 84: 922, 1961) brought some thoughts to my mind. Most certainly the surgeon should receive his just reward for his great responsibility, and I would be the last to deny this. The dramatic factors being what they are in medicine, he usually does. But sometimes the originally correct and early diagnosis, though undramatic, is extremely valuable and should be recognized. Often, too, postoperative care by the attending doctor can be of great value to the patient, and also frequently save the surgeon some valuable time.

There seemed to be some inconsistencies in the report which I have not been able to understand. Why may a clinic group act as a single contractor? Surely the clinic surgeon's fee goes into a pooled income, which is divided, in a manner unknown to the patient, so that the referring doctor eventually receives part of it. The clinics seem happy with this arrangement, yet it is not condoned for private practitioners.

Likewise, medical men in the Department of Veterans Affairs earn about the same per "half-day" as do surgeons, which is another system of "dichotomy". The Royal College also condones this system for its members.

It would seem as if the private practitioner were being conspired against, yet he is the very bulwark of private medical care. When he becomes fed up (and his ranks are growing smaller all the time), socialized medicine will come and the condemned dichotomy will be universal.

I have never practised fee-splitting myself, but have often felt that it would be a fairer method of payment if set up on a proper, uniform basis. It would put the private doctor on a competing basis with his colleagues in the private and union clinics, or D.V.A., and return to him some dignity.

A. C. WALSH, M.D.

99 Victoria Drive,
Vancouver 6, B.C.

AN INTERESTING CASE OF FOOD POISONING

To the Editor:

On May 8 of this year, within 10 minutes of eating what they believed to be wild leeks, at their summer house in the eastern townships, six local gourmets were seized by severe colicky abdominal pain, nausea, vomiting and prostration, and neither their pulses nor their blood pressures were obtainable.

In one case unconsciousness persisted for about 1½ hours. Confusion was a feature in two others. Frequent premature beats and bradycardia were noted, and these could still be detected four to five hours later, even though considerable clinical improvement had occurred.

All the patients improved on a saline-Levophed drip (4 mg./l.) and intravenous corticosteroids, although most of them remained hypotensive for two to four hours. By the following day they all felt completely well and seemed none the worse for their mishap. For two or three days a few red blood cells were seen in the urine, but there was no oliguria.

The plant, which has a bulbous root, not unlike a leek in appearance, and elongated green leaves, is about 8 to 10" in height in the early spring. It was identified by the McGill Department of Botany as *Veratrum viride*.

It was reported by a district farmer to have been the probable cause of the demise of several cows in that area.

All of the patients made a complete recovery.

ADRIAN TOUGAS, M.D.,
MICHAEL NEWHOUSE, M.D.,C.M.,
JOACHIM BRABABDER, M.D.,C.M.

Bedford, Que.

TREATMENT OF SPONTANEOUS PNEUMOTHORAX IN DUSTY OCCUPATIONS

To the Editor:

After a long period of utilization of pneumothorax in the treatment of tuberculosis, during which I have, on several occasions, been forced to establish and maintain pulmonary collapse in the face of an occlusive pleuritis, I wish to submit the following:

Oleothorax was established in a number of cases and I was duly impressed by the development of a moderate pleural thickening. Later, in a number of patients whose occupations were in a dusty environment, such as elevator agents, I was impressed by the repeated recurrence of spontaneous pneumothorax which followed coughing spells actuated by the presence of excess amounts of dust in the respiratory tract. One patient was admitted on three occasions with a spontaneous pneumothorax. I observed the smart reaction of the pleura to the instillation of the small initial fill in establishing an oleothorax to control tuberculosis. It has been considered sound procedure to inject 1 c.c. of 1% Gomenol in Olive Oil into the pleural space. This usually gives rise to soreness in the side for a day or so and some elevation of temperature. When this subsides an obliterative pleuritis follows, and no further spontaneous pneumothorax can take place. This is felt to be of sufficient importance to workers in dusty occupations that it is being reported in the hope that it may obviate lay-offs and frequent repeated hospitalization.

R. W. KIRBY, M.D.

Prince Albert Chest Clinic,
Prince Albert, Sask.

Canad. M. A. J.
July 22, 1961, vol. 85

MEDICAL NEWS IN BRIEF

ALIMENTARY LIPEMIA AND ISCHEMIC HEART DISEASE

Studies on age-matched men have revealed that following fat-feeding, lipemia is more intense and more long-continued in patients with ischemic heart disease than in controls. In Cape Town there reside three racial groups with distinct differences in their customary dietary fat intake: the Bantu, consuming approximately 17% of their calories as fats; the Cape Coloured, approximately 25%; and the European, approximately 40%. Bouchier and Bronte-Stewart (*Lancet*, 1: 363, 1961) set out to determine whether the degree of lipemia following the feeding of fat differed between these racial groups and to compare the findings with those obtained in age-matched patients with ischemic heart disease. In addition the findings following the administration both orally and intravenously of a fat emulsion to a small group of patients with ischemic heart disease were compared with those observed in age-matched controls.

An oral butter-fat tolerance test was performed on 146 males: 29 patients with ischemic heart disease and 117 controls. The controls consisted of members of the three racial groups resident in Cape Town. The alimentary lipemia was greater and more long-continued in patients with ischemic heart disease than in the controls. A typical pattern of tolerance curve was found among the patients: greater fasting lactescence of the plasma and long-continued postprandial lipemia in the patients with ischemic heart disease. No racial or age differences in the fat-tolerance test were demonstrated.

The combined study of oral and intravenous fat-tolerance tests was undertaken on 14 volunteers—seven patients with ischemic heart disease and seven controls. When the fat was fed orally the characteristic differences between patients and controls were observed. When the fat was administered intravenously, no differences in the amount of circulating fat or the rate of removal of the fat from the circulation were detected in the two groups.

PERIPHERAL NEUROPATHY IN RHEUMATOID ARTHRITIS

Widespread recognition of patients with rheumatoid arthritis dying of disseminated necrotizing arteritis has stimulated much interest and controversy regarding the incidence and significance of vascular lesions in rheumatoid arthritis. The clinical feature which has been most constant and distinctive of necrotizing arteritis in its mild as well as its fatal form has been polyneuropathy.

In an effort to establish the comparative incidence of this syndrome before and after the introduction of cortisone or ACTH therapy, a study was made by Ferguson and Slocumb (*Bull. Rheumat. Dis.*, 11: 251, 1961) of all patients with rheumatoid arthritis examined at the Mayo Clinic from 1945 through 1959 for whom a diagnosis of peripheral neuropathy was established. Cases in which neuropathy seemed to have been caused by complicating diseases, such as diabetes, were excluded.

Peripheral polyneuropathy with objective motor loss in patients who had rheumatoid arthritis was found, in the great majority of cases, to be limited to those with severe hypercortisonism. All other forms of neuropathy in rheumatoid patients seemed to be unrelated to the use of adrenal steroids. The type and extent of polyneuropathy had important therapeutic and prognostic implications. Mononeuritis multiplex (motor and sensory impairment in the distribution of two or more individual peripheral nerves) affecting three or four extremities is a manifestation of systemic necrotizing arteritis with a mortality rate of 42%. Less extensive neuropathies with symmetric distal motor impairment or mononeuritis multiplex limited to two extremities often could be proved to be associated with arteritis, but these were accompanied by a good prognosis in respect to recovery.

Gradual reduction of the dose of corticosteroids to near-physiologic maintenance levels is essential for control of hypercortisonism, and should be cautiously attempted in each case whenever manifestations of arteritis are not actively progressing.

GAS GANGRENE FROM ADRENALINE

A particular though remote risk of gas gangrene is involved in administering adrenaline because the vasoconstriction reduces the oxygen tension at the site of injection to a level permitting germination of anaerobic spores. The spread of the infection is rapid, and its nature is often unrecognized until too late. *Clostridium welchii* is the organism invariably found in the infection.

Earlier literature on this subject was almost exclusively Continental; more recently a few cases have been reported in the English and Australian literature. An editorial in the *British Medical Journal* (1: 730, 1961) comments that several interesting facts have come out of recent investigations: (1) Alcohol is incapable of sterilizing syringes; it is unable to kill spores and those of *Cl. welchii* may actually be contained in it. (2) Adrenaline reduces the minimum infecting dose of *Cl. welchii* and of *Cl. septicum* 100,000-fold, but does not reduce that of *Cl. tetani* and of *Cl. histolyticum*. (3) Oily adrenaline does not have any more effect than aqueous adrenaline in enhancing *Cl. welchii* infection. (4) The skin to a considerable distance from the anus is liable to be contaminated with intestinal bacteria of which *Cl. welchii* is a normal member.

Certain conclusions and inferences follow from these facts: (1) Since oily preparations must be injected intramuscularly, and since the risk of gas gangrene is greater after injection by this route, this method of administration is "an unjustifiable risk". (2) Because of the risk of autogenous infection, adrenaline should never be injected in an area close enough to the anus to be contaminated with intestinal bacteria; that is, never in the buttock or thigh.

Some "re-thinking" about the site of injection of immunizing agents, as well as of medicaments, might not be out of place, and when all factors are considered, the subcutaneous connective tissue might be a better depot than muscle for many of these substances.

(Continued on advertising page 27)

THE NINETY-FOURTH ANNUAL MEETING OF THE C.M.A.

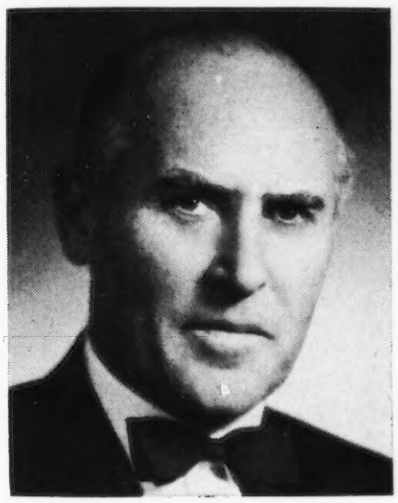
SCIENTIFIC SESSIONS

THE LISTER LECTURE

"BILIARY SURGERY IN SWEDEN"

Hugo Rosenqvist, M.D., Stockholm, Sweden

The twelfth Lister lecture of the Canadian Medical Association was presented in General Session on Thursday, June 22, by Dr. Hugo Rosenqvist, Surgeon-in-Chief of the Södersjukhuset, Stockholm, Sweden.



Dr. Hugo Rosenqvist

Dr. Rosenqvist introduced his discussion of current practices of biliary surgery in Sweden with an interesting commentary describing the introduction of the Listerian principles of antiseptic surgery to Sweden in the latter third of the nineteenth century. Shortly thereafter, the first cholecystectomy was performed by Carl Langenbuch at the Lazarus Hospital in Berlin, on July 15, 1882. In Sweden this operation was performed for the first time seven years later, in 1889. By this time sufficient experience had accumulated in this field of surgery to permit the Swiss surgeon Courvoisier to formulate his famous law, since confirmed by several generations of surgeons, to the effect that: "When the common bile duct is obstructed by a stone, dilatation of the gallbladder is rare; when the duct is obstructed in some other way, dilatation is common."

As late as the year 1900, only six biliary operations had been performed at the Serafimer, one of Stockholm's major hospitals, and all of these were cholecystectomies. The change in the times since then is evidenced by the fact that now more than 1000 cholecystectomies are performed annually in Dr. Rosenqvist's hospital, the Södersjukhuset. Gallbladder disease has become so common in Sweden that it could almost be described as endemic.

Despite intensive research, the etiology of gallstone formation remains a mystery. Similarly, the actual timing and cause for the remarkable apparent increase in prevalence of cholelithiasis in Sweden is unexplained, though it appeared to become evident between 1948 and 1950 when increasing numbers of patients with this disability began to frequent the surgical clinics in that country. The autopsy incidence of gallstones in the 1930's was about 10%. In contrast, one report was published of a postmortem study in 1960, from the largest city in Sweden's richest province, in which it was stated that gallstones were present in 42% of those examined. The increase in cholelithiasis is frequently attributed to the thriving condition of the populace in Sweden's welfare state, but no clear relationship has been established in this respect. Dr. Rosenqvist felt that the difference in the sex incidence of this disease, at different age epochs in men and in women, suggests some hormonal influence, but the nature of this was not defined.

At the Södersjukhuset the number of operations for gallstones increased gradually during the 1940's up to a few hundred cases per year. Since 1950 it has remained relatively constant at 500 to 700 operations per year. Other hospitals throughout Sweden record similar experiences.

The number of cases of gallstones in childhood has also shown a striking increase as exemplified by the experience in one clinic where 59 children between six and 15 years of age were operated upon for gallstones during a recent 10-year period. Only three of these had hemolytic anemia. The etiology of gallstones in childhood is as obscure as that in adults.

The frequency of so-called "silent stones" in Sweden is emphasized by postmortem studies which suggest that between 50% and 80% of those with gallstones have few or no associated symptoms. Even large stones in the common duct, or severe cholecystitis with perforation of stones to adjacent organs, may in some cases cause surprisingly mild clinical manifestations. In about one-quarter of cases of intestinal obstruction due to gallstones no history of biliary disease was evident.

This capricious behaviour makes it difficult to define clear indications for operation. In general, Dr. Rosenqvist advises operation for all *young* persons with abdominal symptoms who show radiological evidence of biliary disease. During the early stages of acute cholecystitis, preferably within seven days of its onset, cholecystectomy should be performed after correction of any disorders of cardiovascular function or fluid balance. In Sweden, it is considered out of date to send such patients home to recuperate from an attack of acute cholecystitis, to return later for subsequent elective cholecystectomy. When the common bile duct is normal and unobstructed, simple cholecystectomy is associated with none of the risks or postoperative complications that may occur after opening and exploring the bile ducts when the latter are inflamed or obstructed.

In one Swedish study for the 10-year period 1950-1959, operations for gallstones and acute or chronic cholecystitis totalled 5340, with a mortality rate of 0.88%. Operations for choledocholithiasis had a mortality of 5%. Uncomplicated cholecystectomies in young and middle-aged patients were associated with a very low mortality rate, most deaths occurring in patients over 60 years of age, with stones in the common bile duct, with jaundice, and with other complicating dis-

Canad. M. A. J.
July 22, 1961, vol. 85

eases, particularly cardiovascular and thromboembolic disorders.

Common duct stones that are overlooked at operation entail a potential risk of subsequent cholangitis, jaundice or pancreatitis in the postoperative period or later. Surgical cholangiography is a procedure of value in minimizing the likelihood of overlooking calculi in the common bile duct at the time of operation and it may also aid in demonstrating other lesions such as tumours, strictures or congenital anomalies. In Sweden this procedure has permitted the diagnosis of stones in the common duct in 16 to 22% of cases so examined. Experience in that country implies that without surgical cholangiography, calculi in the common duct would escape recognition in about every tenth case. It has also demonstrated that stones are present in the intrahepatic ducts in a significantly higher proportion of cases than was previously realized. In addition it aids in mapping out the anatomical details of the duct system and any anomalies therein, providing the surgeon with information of practical value in guiding his operative technique. Therefore, despite certain disadvantages, including the prolongation of operating time, surgical cholangiography is generally viewed in Sweden as a most useful procedure with relatively little risk.

Intravenous cholangiography also has many advantages, but this procedure alone does not suffice to rule out the possibility of stones in the common duct which may be detected by surgical cholangiography even after a negative intravenous cholangiogram. The latter is of value in revealing anatomical anomalies of the ducts, thus permitting the surgeon to avoid any accidental damage to these structures during operation. It also aids in the postoperative detection of stones that may have been overlooked during cholecystectomy.

With the great increase in frequency of biliary surgery in Sweden in recent years, there has been a corresponding increase in the frequency of the serious operative complication of common duct injury which, on the basis of one large survey, occurred in one of every 400 to 450 gallbladder operations. In the Swedish experience these cannot be attributed solely or largely to faulty surgical technique. Many occurred in complicated cases in which the operative technique was hampered by such factors as indurative pericholecystitis, gangrenous perforation of a deep bile duct, and "tenting" of the duct in young, slender persons when it is being exposed during the operation. The latter is a common hazard which deserves more attention on the part of those who perform biliary surgery. If such bile duct injuries are promptly recognized and repaired at the time of operation the prognosis is much better than if their recognition is delayed until biliary peritonitis and postoperative strictures develop later. In repairing these injuries the best results are obtained by end-to-end anastomosis with good apposition of the mucous membrane. Dr. Rosenqvist described in detail the technical procedures involved in repair of ducts damaged at operation, the pathological complications that may follow these injuries and the principles of tube drainage advocated in such cases. The mortality associated with operative injury of the bile ducts, in Sweden, is high, one in every four patients dying as a result of these accidents, most of them in the immediate postoperative period as a result of hepatic insufficiency or other complications.

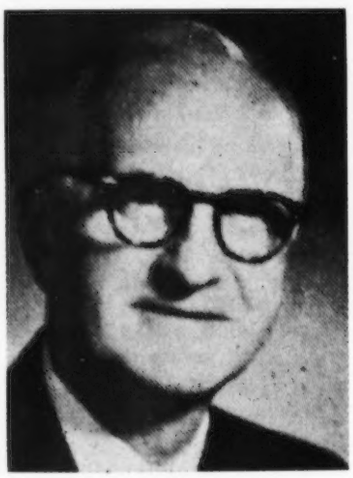
Recently the new technique of transhepatic cholangiography has been introduced in Sweden. It is of particular value in the differential diagnosis of severe jaundice, in which conventional methods of cholangiography are of no avail. This new technique can be used to demonstrate the bile ducts even in the presence of impaired liver function. Under local anesthetic a polyethylene catheter is inserted through a needle into the substance of the liver through the anterior abdominal wall. The needle is withdrawn and the catheter is retained in the liver. Pressure readings can be made through the catheter from the intrahepatic bile ducts and from blood vessels if the tip of the catheter lodges in such vessels. Samples of bile can be obtained for laboratory analysis. After evacuation of bile from the hepatic tree, contrast medium is injected and radiographic studies are made. These usually reveal a vivid and distinct pattern of the biliary ducts. Dr. Rosenqvist recommended that transhepatic cholangiography should be used in patients with operative injuries to the bile ducts to ascertain the anatomic details before re-operation, and in patients with jaundice of obscure etiology, when the surgeon requires information concerning the presence of stone or tumour which is not evident from other forms of investigation.

GENERAL SESSIONS

"THE SWING OF THE PENDULUM"

D. Ewen Cameron, M.D., D.P.M.(Lond.), D.A.B.P.N., F.R.C.P.[C], Montreal

The General Session of Wednesday afternoon, June 21, was chaired by Dr. R. MacGregor Parsons, President of the Association. The opening lecture was delivered by Dr. D. Ewen Cameron, Professor and Chairman of the Department of Psychiatry, McGill University.



Dr. D. Ewen Cameron

In entitling his paper "The Swing of the Pendulum", Dr. Cameron wished to emphasize the changes which have taken place during the last generation in attitudes towards the care of mental illness. In his usual fluent and articulate oratory, he stressed the importance of early recognition of mental illness. The changes in the conception of masturbation and homosexuality represent a transition stage; although these forms of behaviour are not accepted yet, a greater degree of understanding is displayed toward them. Peculiarly, certain patterns of reprehensible mental behaviour on the other hand are still considered commendable socially.

Dr. Cameron said that there is a need for chairs of social psychiatry in universities. By comparison, the rehabilitation of the physically handicapped is far more advanced than that of the psychiatric patient.

It was pointed out that some psychiatrists are either reluctant or unprepared to use all of the different forms of treatment now available in modern psychiatric practice. Nonetheless, at long last, the door is opened for them to do far more for their patients than they were ever able to accomplish in the past.

M. R. DUFRESNE

"THE EFFECT OF X-RAY RADIATION ON THE EMBRYO-FETUS"

Maurice Mayer, M.D., Paris, France

Professor Maurice Mayer of the Faculty of Medicine, University of Paris, reported on the French survey of the effects of radiation on the embryo-fetus. This survey started in 1958 and set out to record the incidence of leukemia, cancers and somatic mutation in children exposed to diagnostic x-radiation while still *in utero*.

Dr. Maurice Mayer

Very few surveyors were involved, and all data were collected from personal interviews with mothers and examination of children. In regard to the leukemias, 100 cases were reported compared with 200 controls. Seven mothers had been subjected to diagnostic irradiation of the pelvis during pregnancy as against four in the control group. When postnatal exposures are added to prenatal ones, the figures are 9:5. In regard to retinoblastoma, 230 cases were reported, compared with 220 controls. Although work is proceeding on this subject, it is still too early to be reported.

With regard to the possible mutagenic effect of ionizing radiation on the fetus, a five-year delay was observed in the collection of data so that some significance could be imparted to the results. In lethal neoplasms a statistically significant difference is found between the irradiated group and the controls ($P = 0.25$). Because of the peculiarity of formation of the pigmented tissue of the iris, heterochromia-iridis was selected as a yardstick for somatic mutations. This abnormality was encountered eight times in 560 children irradiated *in utero* as against two cases out of a group of 2276 controls. Only one case was discovered in the 1696 parents examined. Pigmentary mosaic of the hair was seen in one of the propositi. Results in children are highly significant ($P = 1.8 \times 10^{-6}$).

Dr. Mayer described some of the radiological practices current in his country (chest radiography in the first trimester of pregnancy, placentography, position determination, etc.), and concluded by suggesting a number of improvements in technique designed to reduce exposure of the gonads to x-rays to a minimum.

M. R. DUFRESNE

"THE MEDICAL RESEARCH COUNCIL"

R. F. Farquharson, D.Sc., M.D., LL.D., F.R.C.P.[C], F.R.C.P., F.A.C.P., Toronto

Dr. R. F. Farquharson, Emeritus Professor of Medicine, University of Toronto, Chairman of the Medical Research Council, and Vice-President of the National Research Council of Canada, traced the development of medical research in Canada since the pre-World War I era when any nationally supported research was carried out in various departments of government.

Ashley & Crippen

Dr. R. F. Farquharson

During the First World War, Canada's National Research Council was established as an autonomous body to prosecute research which was at first directed toward facilitation of the war effort. Its earlier work was conducted almost entirely within its own laboratories, but gradually the proportion of its expanding budget diverted to the support of extramural research, including medical research, has increased to a considerable extent since the first government support of extramural medical research related to human illness was provided in 1925 in the form of a grant for the investigation of the efficacy of BCG vaccination. It was not until 1938, however, following the joint request of the Royal College of Physicians and Surgeons of Canada and the Canadian Medical Association, supported by the strong urging of Sir Frederick Banting and Professors J. B. Collip, Duncan Graham, Velyian Henderson and Wilder Penfield, that an Associate Committee on Medical Research was established by the National Research Council. This committee was succeeded in 1946 by the Division of Medical Research of the N.R.C. which was established after the Second World War under the direction of Dean J. B. Collip with Professor Harold Ettinger as Secretary and later Assistant Director. Over the 14 years of its existence, the Medical Division of

Canad. M. A. J.
July 22, 1961, vol. 85

N.R.C. gradually extended its support of medical research, increasing its autonomy with the supervision and guidance of N.R.C. Presidents C. J. MacKenzie and E. W. R. Steacie. Its budget expanded from $200,000 in 1946-47 to $2,300,000 in 1959-1960, its last year of operation.

Soon after the Second World War the need for funds for medical research received increasing recognition throughout the western world, particularly in the United States and to a lesser extent in Canada. The Defence Research Board was established and an appreciable portion of its funds was allocated to medical research. Also about this time the Department of National Health and Welfare made available, through its grants to the Provinces, considerable funds for public health research, and the Department of Veterans Affairs established medical research programs in many of its own hospitals. Substantial sums, which in 1959 amounted to more than two million dollars, were also contributed to medical research by various voluntary and other granting agencies.

Despite this increasing number of granting bodies and the steadily growing financial support of medical research in Canada, the funds available for this purpose were quite inadequate to meet the ever expanding needs. In recognition of this situation the Deans of Canada's medical schools, through the Association of Canadian Medical Colleges, initiated an approach to the Government of Canada that resulted in the appointment of a special committee to review the adequacy of extramural support of medical research by the federal government, and other factors related to this subject. After consideration of the completed report of this special committee the Government of Canada, in 1960, instructed the National Research Council to establish its Medical Research Division as a virtually autonomous subsidiary within the N.R.C. framework, to be called the Medical Research Council, with a view to the possible complete detachment of the subsidiary from its parent body at an appropriate time in the future, should such a course be indicated in the light of subsequent experience.

The Medical Research Council, thus newly created in November 1960, has continued the research program developed by the Medical Division of N.R.C. and has undertaken further careful and continuous study of Canada's needs for the support of research in the broad field of medical science.

At the present time, the Council does not propose to recommend the creation of central medical research laboratories but will direct its resources to support of extramural research in universities, hospitals and like institutions. There is a major need in Canada today for a large number of competent medical scientists comparable to the large staff of able scientists now working in the excellent laboratories of the National Research Council. It is considered that such personnel can best be trained in university centres and their teaching hospitals. There is also an acute need for financial support for the construction of adequate laboratories in these universities and hospitals, and it is of major importance that this need be met soon.

Dr. Farquharson emphasized the need for more direct support from the universities themselves in building up their teaching and research departments, without being obliged to turn to other granting bodies for funds for such purposes.

He expressed the opinion that the various bodies concerned with medical research in Canada such as the Defence Research Board, the Department of National Health and Welfare, the Department of Veterans Affairs and the Medical Research Council, being engaged in different types of activity requiring different emphasis, should continue to operate as independent organizations with individual budgets, since little would likely be gained and much might be lost by placing all their funds in the hands of a single administrative body.

As to its current activities, the Medical Research Council has two major and related functions: (1) the training of medical scientists and the support of highly competent trained investigators engaged in full-time research; and (2) support of operating costs of research programs and the purchase of equipment required for this purpose.

Dr. Farquharson outlined the various categories of medical research personnel now eligible for support from the Medical Research Council. These include summer research scholars, postgraduate medical research fellows, medical research associates, and visiting scientists. He defined in detail the requirements for support under these several categories, their general purpose and function, the nature and conditions of work involved therein, their duration and the range of remuneration available in each personnel category.

He further described the several classes of grants in aid of research that the N.R.C. is prepared to make to medical scientists in universities, teaching hospitals and related scientific institutions in the following categories: annual grants; term grants; major equipment grants; travel grants; and special grants to medical school Deans. He discussed the details of the objectives of each type of grant-in-aid, the terms of eligibility to qualify for such grants and the purposes for which they may be used.

Dr. Farquharson stressed the Council's critical responsibility in the careful examination of all applications for grants and personnel support, in the wise selection of medical research associates and term grantees, and in the provision of optimal support of competent investigators in so far as funds permit. He outlined the techniques by which applications are reviewed and the various subcommittee structures that assist the Council in its examination of applications.

He emphasized the importance of studying the development of young investigators and of encouraging those that do well. Their performance is judged in the end, not by the number, or length, but by the quality of the published results of their research. Though it is easy to recognize the highly competent investigator who develops quickly, it is difficult to be sure that some who flounder at the beginning may not later, through determination to pursue their research, produce excellent work. He cautioned that those who wish to embark on a career of full-time research, such as that supported by the Medical Research Council, must recognize its difficulties and drawbacks and must be motivated by an intense interest in searching for the answers they seek with great patience, persistence and perseverance. This career, he stressed, is not a glamorous hobby, and those not interested in the type of study that it involves or those who lack aptitude for it make little progress and soon tend to become unhappy with their chosen work. For such persons it is as well that they recognize their limitations as research

workers early and devote their lives to some other aspect of the profession.

In conclusion, Dr. Farquharson expressed the hope that the Medical Research Council will develop a program that will attract large numbers of scholars with original minds, and that adequate funds and facilities may be forthcoming to permit them free and full scope for the development of their ideas. We live in an age of technological and scientific explosion, he said, and quoting C. J. MacKenzie, he added that we must run fast to avoid falling behind in the world advance.

"IATROGENIC HAZARDS IN ANESTHESIA"

Leroy D. Vandam, Ph.B., M.D., Boston, Mass., U.S.A.

Under the title "Iatrogenic Hazards in Anesthesia", Dr. Vandam, Clinical Professor of Anesthesia, Harvard Medical School, and Director of Anesthesia, Peter Bent Brigham Hospital, wished to alert physicians to the fact that administration of anesthetics has been complicated in many patients by the increased use of potent

Dr. Leroy D. Vandam

drugs preoperatively in the treatment of such diseases as hypertension, psychiatric illness and arthritis. One of the older drugs, digitalis, is one of the commonest offenders. The dosage of this drug must be carefully tailored to the needs of the patient. This is especially difficult to do, the sicker the patient. The therapeutic dose is 60% of the toxic dose; and the toxic dose is 40% of the lethal dose. Patients who have been digitalized may have received other treatment as well: a low-sodium diet, a tranquillizer preparation, reserpine, a diuretic, ammonium chloride or a sedative. Massive diuresis leading to fluid and electrolyte loss may cause such a patient to come to operation either only partially digitalized or in a state approaching toxicity. Further, patients should not approach operation just after diuresis. It is frequently very difficult to detect symptoms of underdigitalization during operation, and so to decide whether to give more digitalis or not. The anesthetist may be forced to request the surgeon to cancel the operation to avoid an anesthetic fatality.

The preoperative use of tranquillizers, especially phenothiazines (e.g. chlorpromazine), may lead to severe hypotension on the operating table and a subsequent myocardial infarct or stroke. Patients who have been receiving Rauwolfia drugs sometimes develop serious hypotension and cardiac arrest. Reserpine should be discontinued at least two weeks before operation; if this is not possible, the anesthetist should at least be informed so that sympathomimetic drugs may be given during anesthesia.

Adrenal steroids used prior to operation may give rise to adrenal insufficiency in some cases, and circulatory collapse during operation may occur. However, in nine out of ten cases circulatory collapse during operation, in patients who have been receiving adrenal steroids preoperatively, is not due to adrenal insufficiency but to hemorrhage, pulmonary embolism, myocardial infarction or diminished blood volume.

High blood levels of streptomycin, kanamycin or neomycin can cause apnea and hypotension during an operation. This is sometimes noted when a surgeon places a large amount of neomycin in the abdominal cavity. These antibiotics have a synergistic effect in the presence of the muscle relaxants used today. The depressant effects produced can be counteracted by administration of neostigmine.

The prior use of anticoagulants for the treatment of vascular disease may make the administration of local or spinal anesthesia hazardous, in that hemorrhage may be produced by insertion of the injecting needle. The use of chemotherapeutic agents in the treatment of malignant disease, with resultant bone marrow depression, renders a patient extremely susceptible to infection, and creates problems in this sphere with endotracheal intubation and cross-contamination from anesthetic apparatus. The effects of disulfiram (Antabuse) are said to be enhanced by the barbiturates. Certain of the drugs used to treat the various symptoms of Parkinson's disease are alleged to have enhanced anesthetic depressant effects.

It is important that physicians and anesthetists understand these problems so that preventive measures can be taken, certain drugs be discontinued before operation, the patient informed of their hazards and the anesthetist likewise acquainted with the problems. In this manner the anesthetist can be prepared to prevent or treat emergencies of the type described.

"TRANSIENT CEREBRAL ISCHEMIA"

C. Miller Fisher, B.A., M.D., F.R.C.P.[C], Boston, Mass., U.S.A.

In his opening remarks, Dr. C. M. Fisher, Assistant Professor of Neurology, Harvard Medical School, and Neurologist, Massachusetts General Hospital, stated that transitory spells or attacks of central nervous system origin include epilepsy and migraine and another group due to arteriosclerosis and thrombosis. The transitory attacks of numbness, paralysis or dizziness which occur in this latter group are forerunners of a stroke. Diagnosis of this condition enables the physician to initiate therapeutic measures for a disease the only treatment of which is prevention. It is considered less culpable to initiate preventive measures than to await incontrovertible evidence of a stroke.

A single episode of transient hemiplegia or blindness, which clears in hours or days, is generally due to embolism, thrombosis or a small hemorrhage. This condition is not included under the heading of transient cerebral ischemia. Transient cerebral ischemia gives rise to *multiple* and *similar* episodes, which are more *evanescent* (less than 24 hours). They are due to local transient ischemia and never to hemorrhage, infarct

Canad. M. A. J.
July 22, 1961, vol. 85

or embolism. The attacks may last from a few seconds to one to 10 minutes to hours. One attack alone may precede a stroke or there may be hundreds of spells days or weeks before a stroke, or a stroke may not even occur. There is no way of predicting the course and outcome.

The sites of involvement in order of frequency are: the carotid sinus; the top of the vertebral arteries; and, much less commonly, the bifurcation of the middle cerebral artery, and the vertebral arteries as they arise from the subclavian vessels. In regard to the carotid sinus site, weakness, paralysis, numbness of the opposite side of the face, tingling and dizziness are frequent findings. Motor involvement predominates over sensory. Visual scintillation is not an associated finding, nor do these patients go on to have seizures.

Dr. C. Miller Fisher

Patients affected in the second most common site, the basilar-vertebral distribution, exhibit dizziness, wobbling gait and dimmed vision. Diplopia, dysarthria and hemiplegia also occur. Memory loss may be present (because of hippocampal involvement); attacks of quadriplegia may occur (but not as an isolated finding); headache is common; focal convulsions do not occur; and loss of consciousness is extremely rare. Some rarer findings include hemiballismus and peduncular hallucinosis.

The major pathological feature is ischemia, and since transient cerebral ischemia bears a relation to an on coming stroke, the arterial lesion is, as might be expected, atherosclerosis with thrombosis, giving rise to stenosis of the lumen. Postmortem studies have not been very helpful, since the patient rarely dies at the time of the attack. Arteriographic studies have been of the greatest value. The next step in research investigation will be thorough examination of the lumen of the vessel after endarterectomy; the *whole* specimen in carotidectomy should be sent to the pathology laboratory for sectioning.

Stenosis is the basis of the disease, but this of itself does not explain the intermittency of transient cerebral ischemia. As early as 1911, Osler reported a case in this Journal (*Canad. M. A. J.*, 1: 919, 1911) of transient attacks of aphasia, monoplegia, and hemiplegia extending over four or five years; he favoured vasospasm as the cause.

Others have thought that hypotension was the better explanation.

It is known that use of anticoagulants will prevent these attacks in a large number of patients. This would suggest the importance of thrombosis as having a causative role. However, use of anticoagulants does not stop all attacks. It may be that anticoagulants affect the collateral flow rather than merely the thrombus formation.

The majority of episodes of transient cerebral ischemia occur when the patient is up and around, rather than when reclining, especially in the morning after rising or after breakfast; and on standing up or after a hot bath, rather than while lying down. To awaken to one is uncommon. It would seem that the reduced circulation of sleep converts a potential episode of transient cerebral ischemia to a stroke.

Examination of the retina during an attack of blindness has revealed a white mass at the bifurcation of the central retinal artery. During the next 45 minutes the mass was seen to move to one of the temporal branches of the retinal artery. It took an hour for it to disappear. Some sort of coagulum would seem to be responsible.

There must therefore be more than one possible etiology of transient cerebral ischemia: hypertension (possibly); stenosis in association with thrombus formation (presumably, anticoagulants interfere with the development of this process); and coagulum formation.

In general, loss of consciousness, generalized seizures, and transient loss of memory do not occur in transient cerebral ischemia. Dizziness alone is not an indication for use of anticoagulants. Similarly, scintillation or visual flicker, which is common in middle age and in the elderly, is generally benign and is not an indication for administration of anticoagulants.

(*To be continued*)

PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

CANADIAN MEDICAL ASSOCIATION ANNUAL MEETING, MONTREAL, 1911

The forty-fourth annual meeting of the Canadian Medical Association was held in Montreal, June 7th, 8th, and 9th, 1911. The president, Dr. George E. Armstrong, presided, and there were present 418 registered members.

The Association met in the new building which has been erected for the faculty of medicine of McGill University. The opening meeting began at 10.30 a.m. on Wednesday, June 7th, with an invocation by the Rev. Herbert Symonds, D.D., Vicar of Christ Church Cathedral. The president-elect was installed, and addresses of welcome were given by His Worship the Mayor and by Principal Peterson of McGill University.

The report of the chairman of the committee of management was read. The general secretary read the minutes of the last meeting, and the election of members to the executive council was proceeded with.

Nominations being called for, it was moved, seconded, and carried that as many of the old council as were present should be re-elected. These were: Dr. G. E. Armstrong, Montreal; Dr. Ingersoll Olmsted, Hamilton; Dr. F. N. G. Starr, Toronto; Dr. J. H. Elliott, Toronto; Dr. John Stewart, Halifax; Dr. A. McPhedran, Toronto; Dr. R. A. Reeve, Toronto; Dr. Murray Maclaren, Saint John; Dr. Alexander McNeill, Summerside, P.E.I.; and Dr. F. G. Finley, Montreal. Of these, Dr. Geo. E. Armstrong, as president, was considered a member *ex officio*, so that nine of the old members were considered re-elected. The nomination of six new members was then proceeded with.—*Canad. M. A. J.*, 1: 625, 1911.

ASSOCIATION NOTES

EXECUTIVE COMMITTEE MEETING,

June 16 and 17, 1961

The Executive Committee of the Canadian Medical Association met in the Harricana Room of the Queen Elizabeth Hotel, Montreal, preliminary to the opening of the Ninety-Fourth Annual Meeting of the Association.

Following the roll call, the Chairman welcomed Dr. René DuBerger of Chicoutimi, Quebec, Dr. H. D. Dalgleish of Saskatoon, and Dr. L. R. Rabson of Winnipeg, who attended as observers. Dr. T. Primrose of Montreal also attended a portion of the meeting as an observer.

Canadian Medical Association Medal of Service

Dr. E. Kirk Lyon, reporting on his discussion with Dr. R. M. Janes, Chairman of the Committee on Awards, Scholarships and Lectures concerning the creation of a C.M.A. Award in the form of a gold medal as described in the minutes of previous Executive Committee Meetings, stated that agreement had been reached concerning the establishment and terms of such an award, to be known as The Canadian Medical Association Medal of Service. Only one such medal may be presented each year and the Association shall be under no obligation, in any year, to make this award. Nominations are to be made in writing by any member of General Council and, accompanied by a pertinent citation stating the reasons for the nomination, are to be submitted to the Committee on Awards, Scholarships and Lectures at least six months before the annual meeting at which the medal is to be presented. After reviewing the nominations, the Committee on Awards, Scholarships and Lectures shall present their recommendations to the Executive Committee at a meeting of that Committee at least one month prior to the annual meeting of General Council. The Executive Committee shall be empowered by General Council to reject or approve, on behalf of Council, the recommendations of the Committee on Awards, Scholarships and Lectures. The recipient of the Award shall be offered the opportunity of attending the Annual General Meeting for its acceptance, at the expense of the C.M.A. In case of the demise of the nominee after his selection but prior to its presentation, the Award shall be presented posthumously. The following conditions will govern the selection of recipients of The Canadian Medical Association Medal of Service: (1) service to the profession in the field of medical organization; (2) service to the people of Canada in raising the standards of medical practice in this country; (3) personal contribution to advancement of the art and science of medicine; (4) to qualify, a recipient must have made contributions in at least two of the foregoing fields.

These recommendations were accepted by the Executive Committee.

Finance Committee Report

At its last meeting the Executive Committee instructed that expert opinions be obtained as to the size and requirements of the Association's General Reserve Fund. Accordingly, opinions were obtained from Mr. Knight, the Association auditor, and Mr. Wilson of the Royal Trust Company, the Association's financial advisers. The Finance Committee met to consider their recommendations. As a result of these deliberations the Finance Committee brought down a detailed report thereon, together with a projected 10-year budget based on past experience. After some discussion of the Finance Committee's report the Executive Committee approved the following proposals concerning future financial policies of the Association: (1) That a minimum unallocated general reserve fund of $200,000 be maintained, recognizing that this will increase with Association activities of the next few years. (2) That a sum of $40,000 be set aside for the allocated building fund reserve, commencing in 1961-62; and that for 1960-61 the amount designated for this purpose shall be $25,000. (3) That a policy be established whereby future reserves shall be invested in securities approved by Canadian Life Insurance Companies, excepting only common and preferred stocks. (4) That an increase in membership fees be recommended at the end of 1962 or not later than 1963 and that this should be borne in mind by the Divisions of the Association in any consideration of an increase in their fees which might coincide with the foregoing. (5) That profits from the C.M.A. publications to be diverted to the general fund, be projected on a basis of 10% of the annual financial turnover of the publications department, provided that such action in no way impairs the proper conduct and reasonable expansion of the publications department, and that the quality of the Association's journals is, in principle, to take precedence over financial profit therefrom.

CAMSI Foundation for Loans and Bursaries

As recorded in reports of previous Executive Committee meetings, the Committee entertains reservations concerning the soundness of the methods proposed by the Canadian Association of Medical Students and Interns for the creation of a Foundation to provide financial assistance in the form of loans and bursaries for undergraduate and postgraduate medical training. Although this opinion was transmitted to CAMSI, it is understood that that Association proposes to proceed with the incorporation of such a Foundation under letters patent and that proceedings have been instituted to this end. The president of CAMSI had corresponded with the General Secretary of the C.M.A. requesting the opportunity to publicize the details of the plans to establish the CAMSI Foundation at the forthcoming annual meeting of the C.M.A. It was agreed that the president of CAMSI or his representative should be invited to discuss this matter with the Executive Commitee before the completion of its present meeting. No response to this invitation was forthcoming.

Progress Report of the Executive Subcommittee on Health Services

Dr. G. E. Wodehouse, Chairman of the Executive Subcommittee on Health Services, reported that that body had been hampered in its activities by the lack of terms of reference for the proposed Royal Commission

Canad. M. A. J.
July 22, 1961, vol. 85

on Health Services. Progress was reported concerning the Secretariat's continuing studies of the current state of medical manpower in Canada. In recent correspondence with the Prime Minister, the Executive Subcommittee stressed the desire and intent of the C.M.A. to carefully prepare the most effective contribution which the Association can make toward the objectives of the Royal Commission on Health Services. It was pointed out that such efforts would of necessity be based on a knowledge of the Commission's terms of reference, about which no definite information was available when this correspondence was directed to Mr. Diefenbaker. The Executive Subcommittee on Health Services considered it desirable and diplomatic to publicly record the action of the C.M.A. in expressing its desire to forward the objectives of the Royal Commission on Health Services, and felt that the most appropriate way to present this information to the public would be through the President's Valedictory Address. The latter was therefore amended in keeping with this recommendation. The Executive Subcommittee plans to maintain close liaison with the Divisions in respect of their planning of submissions for presentation before the Royal Commission and had arranged to meet with Divisional representatives responsible for the preparation of such briefs, during the week of the 94th Annual Meeting. The Subcommittee also planned to meet in mid-July to deliberate on the terms of reference of the Royal Commission on Health Services, assuming that these would be released by that time, and to confer again with Divisional representatives of the C.M.A.'s affiliated societies. It was reported that members of the Executive Subcommittee would hold informal discussions during the forthcoming week with Chief Justice Hall, Chairman of the Royal Commission on Health Services.

Report from Saskatchewan

Dr. H. D. Dalgleish reported that the Saskatchewan Advisory Planning Committee on Medical Care, under pressure to bring in a report at an early date, is stepping up its activities with the aim of presenting by early September an interim report concerning only that phase of its program dealing with the provision of physicians' services to all citizens of Saskatchewan. This sense of urgency and haste apparently does not apply to other aspects of the Advisory Planning Committee's report. The College of Physicians and Surgeons of Saskatchewan has been invited to hold further meetings with the Advisory Planning Committee and arrangements are being made to hold such meetings at an early date. The representatives of the College consider that such discussions will likely involve the subjects of universal compulsory health services coverage for all citizens of Saskatchewan, government control of these services, the costs involved and the attitude of the Saskatchewan medical profession toward these matters. Dr. Dalgleish requested some further guidance for the Saskatchewan Division representatives in order that their approach to these problems remain in accord with the views and policies of the C.M.A. in general. He stressed the problems involved in properly and adequately informing the public concerning the medical profession's views. He noted that Saskatchewan doctors are prepared to adopt the stand that they oppose the principle of dealing with any third party concerning remuneration for their services and hold the conviction that they should deal only with their patients in this regard. In the event that government-controlled universal health insurance is enacted, the profession's stand would involve the principle of refund of payments, hitherto unprecedented in Canada.

The Executive Committee then decided that the following statement should be incorporated in the discussion of that portion of its Report to General Council dealing with the Saskatchewan situation:

"The C.M.A. wishes to express its concern that political pressures in the Province of Saskatchewan may be exerted on the Advisory Planning Committee on Medical Care of that province to hasten its recommendations concerning medical services insurance before the studies and deliberations of the Committee have been brought to an orderly conclusion.

"It is the opinion of the C.M.A. that medical services insurance can only be considered properly in its relationship to all other aspects of health services. It is also our opinion that it might not be in the best interests of either the citizens of Saskatchewan or of the citizens of the remainder of Canada if a pattern of governmental medical services insurance should be established prematurely in that province."

The 94th Annual Meeting

The Deputy General Secretary outlined arrangements for the forthcoming sessions of General Council, scientific sessions, annual general meeting, the Economics Day program, social events and public relations arrangements. After some discussion it was agreed that members of General Council should be seated in alphabetical order, rather than in Divisional groups, the object of such seating arrangement being to minimize any tendency to sectionalism in the voting and discussion at the meeting of General Council.

Medical Care in Extended Treatment Hospitals and Facilities

Dr. Wm. Baldwin, as a C.M.A. representative on the Joint C.M.A.-Canadian Hospital Association Committee appointed to investigate the problems of providing adequate medical care for patients in extended treatment facilities, reported on the deliberations of the Joint Committee to date. It is the general view of the profession that remuneration of physicians involved in the provision of medical services to patients in such facilities should not be administered as an extension of the Hospital Services Insurance Act, and this view was impressed on the C.H.A. representatives to the Joint Committee. Alternative ways and means of providing remuneration for medical services to persons in institutions for the chronically ill, aged and disabled were deliberated at length by the Joint Committee, and the complexities and difficulties of this subject were recognized. No final recommendations or proposals have as yet arisen from these discussions, though there was general agreement that the present hit-and-miss method of providing such services is unsatisfactory and that it would be preferable to provide proper quality and continuity of medical care by an officially appointed medical staff who would be remunerated on the basis of the services they contribute to such a program. The mechanism by which this remuneration would be provided was not defined.

The importance of adopting a system that would provide for continuity of medical care and supervision of such patients before admission to long-term insti-

tutions, throughout their residence in the institution, and in their after-care, was emphasized in the discussion. Difficulties in ensuring care of institutionalized patients by their private physicians was also stressed. The Canadian Hospital Association is of the opinion that the most effective way of providing medical care to patients in extended treatment facilities is by payment of appointed institutional staff physicians through the mechanism of the Hospital Services Insurance Act. The Department of National Health and Welfare, however, is not prepared to authorize funds for this purpose until both the C.M.A. and C.H.A. expressed their agreement to such a procedure.

The Executive Committee approved the principle that the provision of medical care for patients in long-term or chronic institutions should be accomplished through an organized, appointed medical staff, not necessarily a "closed" staff. This proposal was adopted in the form of a motion, in discussion of which it was brought out that this principle does not exclude the care of patients in such institutions by their own private physicians, nor does it consider the matter of remuneration of physicians for such services.

The Executive Committee also voted approval of a motion asserting that the C.M.A. affirms its opposition, at this time, to payment for the professional component of medical care for patients in institutions for the aged, chronically ill or disabled under terms of the Hospital Service Insurance Act, but recommends that other methods of payment for such services be investigated by individual Divisions of the Association.

Mental Health Survey in British Columbia by a Committee of the American Psychiatric Association

Dr. R. O. Jones reported that there was considerable dissatisfaction on the part of certain Canadian bodies in connection with the limited degree to which they have been involved in the recently reported survey of mental health in B.C. that was conducted by a committee of the American Psychiatric Association, and that many Canadian physicians feel that they did not have adequate opportunity to participate in the investigation on which this report was based. As a consequence the Canadian Mental Health Association has dissociated itself from the authorship of this report.

The Executive Committee directed the General Secretary to consult with Dr. Alan Gilbert, the C.M.A. representative on the study group who conducted the survey in question, to determine whether the C.M.A. should or should not dissociate itself from sponsorship or participation in the authorship of the survey report.

The Executive Committee also

—Accepted without comment the reports to General Council of the Committees on Medical Education and Rehabilitation, which were not available at the previous Executive Committee meeting.

—Accepted the offer of Dr. Hager Hethrington to represent the C.M.A. at the meeting of the Medical Association of South Africa, Cape Town, September 24-30, 1961.

—Approved the General Secretary's acceptance of an invitation to address the Canadian Pharmaceutical Convention in Hamilton, Ontario, August 14, 1961, on the subject of the provision of medical care services in different countries.

—Received for information the Staffing Committee's report that Dr. J. O. Godden had joined the staff as an Associate Editor of C.M.A. publications on June 1; that Mr. Guy Clarkson had reported for duty as Economist and Statistician in the Department of Medical Economics on June 5; and that negotiations to obtain the services of an appropriately qualified solicitor to the C.M.A. would be pursued.

—Appointed Dr. Gilbert Turner, Dr. Roger Dufresne and Dr. Guillaume Gill as C.M.A. representatives to attend a forthcoming conference to explore the subject of standards for training and qualifications of inhalation therapists.

—Referred to the incoming Executive Committee: (a) An invitation to appoint a representative of the C.M.A. to attend the meeting of the recently formed Australian Medical Congress (previously the Australian Branch of the British Medical Association) at Adelaide, May 19-25, 1962. (b) The appointment of a C.M.A. representative on the Canadian Council of Nutrition to replace Dr. Harding leRiche whose term expired June 30, 1961. (c) A communication from the Manitoba Division raising the question of extension of C.M.A. endorsation to the Royal College of Physicians and Surgeons' statement concerning itinerant surgery. (d) A communication from the President of the B.C. Division concerning the future leadership of the profession and the method of selection of the Association's officers.

—Referred to the Committee on Medical Education a communication from the Canadian Psychiatric Association concerning the qualifications of foreign medical graduates who wish to come to Canada for psychiatric training and/or practice:

—Referred to the Committee on International Affairs a communication from Canadian Overseas Volunteers requesting that the C.M.A. sponsor a Canadian physician for a one-year period of service in India, by a contribution of $2000.

—Referred to the Committee on Committees the duty of appointing three delegates from the C.M.A. to meet with representatives of the Emergency Health Services (successor to the Defence Medical and Dental Services Advisory Board) as a Co-ordinating Committee to draw up a guide for training of auxiliary health personnel to organize and handle programs to be used in the event of natural or military disasters.

—Received for information a letter from the Canadian Red Cross Society expressing the gratitude of that organization for the co-operation and support of the C.M.A. toward the disaster programs in Morocco and the Congo.

The Chairman of the Executive Committee then expressed personal messages of thanks to each of the retiring members of the Committee for their past contributions. Those whose term on the Committee has expired are Drs. Lyon, Lehmann, Haig, Stewartson, Baldwin, Lemieux and Quintin, although Dr. Quintin almost immediately returned like a good penny, in the garb of the newly elected Chairman of General Council.

The date for the next meeting of the Executive Committee was established as June 22, the meeting to be held in the Queen Elizabeth Hotel, Montreal, after completion of the sessions of General Council.

Canad. M. A. J.
July 22, 1961, vol. 85

EXECUTIVE COMMITTEE MEETING,

June 22, 1961

The incoming Executive Committee met in the Chaudière Room of the Queen Elizabeth Hotel, Montreal, on June 22.

After the roll call and introduction of new members as listed in the report of the 1961 Meeting of General Council (*Canad. M. A. J.*, 85: 157, 1961), Dr. T. J. Quintin of Sherbrooke, Quebec, Chairman of General Council, was elected Chairman of the Executive Committee by unanimous vote.

Report of the Committee on Committees

The Executive Committee then approved the appointment of the following Standing Committees, Special Committees and C.M.A. representatives on other organizations:

Standing Committees

Advisory Committee to the Federal Government—Dr. T. J. Quintin—Chairman; Dr. F. S. Hobbs, Vancouver; Dr. R. F. DuBerger, Quebec; Dr. G. E. Wodehouse, Toronto; Dr. J. F. McInerney, Fredericton; Dr. L. R. Rabson, Winnipeg; Dr. J. A. McMillan, Charlottetown; Dr. G. W. Halpenny, Dr. A. D. Kelly—ex officio.

Committee on Archives—Dr. H. E. Rawlinson, Edmonton.

Committee on Awards, Scholarships and Lectures—Dr. R. D. Kerr, Vancouver—Chairman.

Committee on By-laws—Dr. M. O. Klotz, Ottawa.

Committee on Cancer—Dr. R. C. Harrison, Edmonton.

Committee on Child Health—Dr. L. C. Grisdale, Edmonton.

Central Program Committee—Dr. R. C. Laird, Toronto.

Committee on Economics—Dr. J. A. McMillan, Charlottetown—Chairman.

Committee on Ethics—Dr. Wallace Wilson, Vancouver.

Committee on Hospital Service and Accreditation—Dr. N. N. Levinne, Toronto—Chairman; Dr. J. R. Francis, Calgary; Dr. H. Paul Melanson, Moncton; Dr. B. H. McNeel, Toronto.

Committee on Income Tax—Dr. N. J. Blair, Vancouver—Chairman; Dr. M. O. Klotz, Ottawa; Dr. T. Primrose, Montreal; Dr. K. R. Trueman, Winnipeg; Dr. G. E. Wodehouse, Toronto, Dr. A. D. Kelly, Toronto—ex officio.

Committee on Approval of Hospitals for Training of Junior Interns—Dr. L. O. Bradley, Winnipeg—Chairman; Dr. D. F. Cameron, Edmonton; Dr. A. F. W. Anglin, Toronto; Dr. R. Dufresne, Montreal; Dr. D. I. Rice, Halifax; Dr. E. W. Nancekivell, Hamilton; Dr. Lea C. Steeves, Halifax.

Committee on Approval of Schools for Laboratory Technologists—Dr. D. F. Moore, Saskatoon—Chairman; Dr. H. G. Pritzker, Toronto; Dr. J. Eden, Vancouver; Dr. Ian A. MacLennan, Moncton; Dr. D. W. Penner, Winnipeg; Dr. D. Hugh Starkey, Montreal.

Committee on Maternal Welfare—Dr. Louis J. Harris, Toronto.

Committee on Medical Education—Dr. A. F. Hardyment, Vancouver.

Committee on Nutrition—Dr. W. Harding leRiche, Toronto.

Committee on Occupational Medicine—Dr. D. K. Grant, Toronto.

Committee on Pharmacy—Dr. M. Nickerson, Winnipeg.

Committee on Physical Education and Recreation—Dr. G. E. Duff Wilson, Kitchener.

Committee on Public Health—Dr. Wm. Watt, Winnipeg.

Committee on Public Relations—Dr. F. A. Dunsworth, Halifax.

Committee on Approval of Schools for Radiological Technicians—Dr. J. G. Stapleton, Hamilton.

Committee on Rehabilitation—Dr. Gustave Gingras, Montreal.

Committee on the Medical Aspects of Traffic Accidents—Dr. Wallace Troup, Ottawa.

Special Committees

Liaison Committee with l'Association des Médecins de Langue Française du Canada—Dr. G. W. Halpenny, Montreal—Chairman; Dr. J. R. Lemieux, Quebec; Dr. J. H. M. Rice, Campbellton.

Committee on C.M.A. Organization—Dr. R. O. Jones, Halifax—Chairman; Dr. J. B. Roberts, St. John's; Dr. E. F. Donald, Edmonton.

Editorial Board—Dr. D. C. Graham, Toronto—Chairman.

Finance Committee and Nucleus of Trusteeship Committee—Dr. G. E. Wodehouse, Toronto—Chairman; Dr. T. Tweed Samis, Toronto; Dr. E. W. Mitchell, Toronto.

House Committee—Dr. T. C. Routley, Toronto—Chairman; Dr. A. D. Kelly; Dr. A. F. W. Peart; Mr. B. E. Freamo; Mr. C. M. Reside.

Committee on International Relations—Dr. M. A. R. Young, Lamont—Chairman.

Committee on Prepaid Medical Care—Dr. L. R. Rabson, Winnipeg—Chairman; Dr. J. Howard Black, Vancouver; Dr. D. F. McPherson, Lethbridge, Dr. G. E. Wodehouse, Toronto; Dr. R. M. Anderson, Toronto; Dr. P. Bruce Lockhart, Toronto; Dr. T. J. Quintin—ex officio.

Executive Sub-Committee on Health Care—Dr. G. E. Wodehouse, Toronto—Chairman; Dr. J. A. McMillan, Charlottetown; Dr. L. R. Rabson, Winnipeg.

Committee on Relative Value Studies—Dr. R. M. Janes, Toronto—Chairman; Dr. W. E. Armour, Toronto; Dr. R. S. Braiden, Toronto; Dr. D. E. Cannell, Toronto; Dr. J. Gollom, Toronto; Dr. D. J. Mackenzie, Toronto; Mr. B. E. Freamo, Toronto—ex officio.

Staffing Committee—Dr. G. E. Wodehouse, Toronto—Chairman; Dr. R. W. Richardson, Winnipeg; Dr. T. C. Routley, Toronto.

C.M.A. Representatives on Outside Bodies

Association of Canadian Medical Colleges—Dr. A. F. Hardyment, Vancouver.

Canadian Conference on Health Care—Dr. J. A. McMillan, Charlottetown; Dr. A. D. Kelly, Toronto.

Canadian Council on Hospital Accreditation—Dr. N. N. Levinne, Toronto; Dr. J. R. Francis, Calgary; Dr. H. Paul Melanson, Moncton; Dr. B. H. McNeel, Toronto.

Canadian Council on Nutrition—Dr. W. Harding leRiche, Toronto.

Emergency Health Services Advisory Committee—Dr. J. H. Gibson, Sarnia—Chairman; Dr. T. L. Fisher, Ottawa; Dr. R. J. Weil, Halifax.

Liaison Committee with Canadian Pharmaceutical Association—Dr. M. Nickerson, Winnipeg; Dr. E. K. Lyon, Leamington; Dr. T. C. Routley, Toronto.

Liaison Committee with the Canadian Psychiatric Association—Dr. M. Dufresne, Montreal—Chairman; Dr. R. Rolland, Montreal; Dr. C. B. Solursh, Toronto.

Health League of Canada—Dr. W. G. Watts, Toronto.

Canadian Commission on Nursing—Dr. H. T. Ewart, Hamilton; Dr. Paul Bourgeois, Montreal; Dr. M. A. R. Young, Lamont; Dr. A. F. W. Peart, Toronto—ex officio.

National Cancer Institute—Dr. N. H. Gosse, Halifax; Dr. Carleton B. Peirce, Montreal; Dr. R. C. Harrison, Edmonton.

Physicians' Art Salon—Dr. G. E. Tremble, Montreal—Chairman; Dr. G. Harvey Agnew, Toronto; Dr. Arthur L. Murphy, Halifax.

Canadian Society of Radiological Technicians—Dr. J. G. Stapleton, Hamilton.

National Advisory Committee on Rehabilitation of Disabled Persons—Dr. Gustave Gingras, Montreal.

Drug Advisory Committee (Dept. of National Health and Welfare)—Dr. R. Dufresne, Montreal; Dr. M. Nickerson, Winnipeg.

Trans-Canada Medical Plans—Dr. J. A. McMillan, Charlottetown; Mr. B. E. Freamo, Toronto.

Victorian Order of Nurses—Dr. J. H. B. Hilton, Ottawa.

Appointment of Financial Adviser

Retention of The Royal Trust Company as Financial Adviser to the Association was unanimously approved.

Business Referred from General Council

The following action was taken with regard to the resolutions referred to the Executive Committee from General Council:

"That this Council urges T.C.M.P. to align itself with those bodies which have a common interest in the provision of medical services insurance on a voluntary basis, by becoming a participating member in the Canadian Conference on Health Care."

Dr. J. A. McMillan was directed to bring this resolution to the attention of the T.C.M.P. Commission at its meeting later in the same day.

"That the C.M.A. employ as many individuals as necessary to complete the relative value schedule with all possible despatch."

This resolution was referred to the Committee on Relative Value Studies.

"That a copy of the C.M.A. Statement on Medical Services Insurance be suitably prepared and distributed to all members of the medical profession in Canada."

The Committee agreed that this action be taken by the Secretariat.

"That Council instruct the Committee on Economics and the Executive Committee to review the terms of reference of T.C.M.P. to ascertain whether or not this organization under its present terms of reference is capable of serving the Canadian Medical Association in providing a broadened coverage for the Canadian public in the field of benefits provided and the expansion of the numbers covered, as expeditiously as possible."

This resolution was referred to the Committee on Economics.

"WHEREAS *a more frequent interchange of ideas regarding the economics of medical care is desirable within the Divisions of The Canadian Medical Association,*

"THEREFORE BE IT RESOLVED *that the Council recommend to the Executive Committee that teams dealing with the economics of medical care be made available to Divisional meetings in order that an interchange of ideas across Canada be thereby facilitated."*

The Committee directed that a memorandum be circulated to the Divisions, informing them of the interpretation placed on this resolution by the Executive Committee.

"That a joint committee be set up, consisting of the C.M.A. and those affiliated specialist societies who are interested in studying the problem of technical education and its relationship to medical services with particular reference to the so-called 'internship' following training in central schools."

The Executive Committee instructed the Secretariat to delineate the various bodies to whom this resolution applies and to report back to this Committee for further action.

"That this General Council recommend to the Executive Committee that the question of relationship between the active members of medical staffs to boards of administration of hospitals be studied by the C.M.A."

This resolution was referred to the Committee on Hospital Accreditation.

"WHEREAS *there are now provincial Tumour Registries or nuclei for provincial Registries in all provinces,*

"THEREFORE BE IT RESOLVED THAT *this Council recommends the formation of a complete national Tumour Registry in Ottawa.*

"BE IT FURTHER RESOLVED *that the co-operation of the National Cancer Institute, Canadian Cancer Society, Dominion Bureau of Statistics and the medical profession of Canada be sought to develop this national Registry as soon as possible with exploration of the possibility of financing this through Federal-Provincial Grants."*

This resolution was referred to the Committee on Cancer, who are to be advised that the General Secretary, on behalf of the Executive Committee, is informing the bodies named in the resolution of the proposal contained therein, as an expression of C.M.A. opinion.

"Your Cancer Committee move that Council authorize us to work in co-operation with the National Cancer Institute to establish a program of clinical trials in Canada and that the Council allocate the sum of $8000 from the King George V Fund for this purpose."

The Executive Committee voted the adoption of this resolution and authorized the action proposed therein.

"Resolved that this Association should do all within its power, by democratic means, to oppose any arbitrary act of government which imposes classification of members of the medical profession, in whole or in part, as civil servants, against their will."

The Executive Committee voted the adoption of this resolution.

"That General Council recommends to the Executive Committee that past Chairmen of General Council be recognized in the same way as Past Presidents of the Association in so far as their participation in and attendance at official activities of General Council are concerned."

This resolution was referred to the Committee on By-Laws.

Business Referred from the 1960-1961 Executive Committee

Definition of this Committee's comments and recommendations concerning the proposed creation of a CAMSI Foundation for provision of loans and bursaries was deferred until further information on this subject is available from the incoming executive of CAMSI.

The Executive Committee approved by vote the policy that attendance of non-Committee members as observers at its meetings should be restricted to (a) alternates of Committee members if their attendance is requested by the Division concerned, subject to consent by the Chairman of the Executive Committee, (b) Chairmen of other committees specifically invited to attend individual meetings of the Executive Committee, subject to concurrence by the Executive Committee Chairman, and (c) members of the staff of the Association, under supervision of the General Secretary.

The Executive Committee voted support of the recommendation by General Council that it give sympathetic consideration to any request from the Newfoundland Division for financial assistance toward expenses

Canad. M. A. J.
July 22, 1961, vol. 85

incurred in its approach to the problem of defining the legal status of Newfoundland cottage doctors.

A communication from the Manitoba Division which raised the question of extension of C.M.A. endorsation of the statement concerning itinerant surgery, promulgated by the Royal College of Physicians and Surgeons of Canada, was referred to the C.M.A. Committee on Ethics.

World Medical Association

The Chairman introduced Drs. Morley Young and A. F. VanWart, C.M.A. delegates to the 15th W.M.A. Assembly at Rio de Janeiro in September 1961. Dr. Young outlined the present status of the deliberations of the special study committee that was appointed to investigate the functions, objectives and programs of W.M.A. He commented on the recent appointment of Dr. Harry Gear of South Africa to replace Dr. Heinz Lord as Secretary-General of W.M.A. after Dr. Lord's untimely death. He urged the support of all member Associations in arranging for the settlement of refugee doctors, and announced the creation of a new W.M.A. region, to be known as the African Region.

Dr. Young also commented on the quality of the World Conference on Medical Education which was held in Chicago approximately two years ago and recommended that the Proceedings of this Conference be referred to the C.M.A. Committee on Medical Education. He anticipated that the C.M.A. will likely be requested to make its usual contribution toward the advancement of world medicine and suggested that the amount of $10,000 for the current year would be in order in this respect.

The Executive Committee's previous action in providing for continuity in liaison with W.M.A., by designating a member of the Secretariat to accompany the delegates to the annual W.M.A. Assemblies, was felt to be highly desirable.

The Committee requested the delegates to convey to the W.M.A. Assembly this Association's belief that its activities in international medicine should be concentrated in W.M.A. rather than in narrower groups such as the proposed Commonwealth Medical Association.

Dr. T. C. Routley observed that he had sensed an undertone of unrest in certain circles in the World Medical Association in the past, to the point at which some of the major national member groups were considering withdrawal from the Association. He expressed the hope that this situation might be alleviated with Dr. Gear's appointment as Secretary-General.

The Executive Committee also

—Received for information a report of preliminary arrangements for the 95th Annual Meeting which will be held in Winnipeg, June 17-23, 1962.

—Granted authority for the completion of business arising out of all portions of the 94th Annual Meeting.

—Recommended acceptance of the application for affiliation from the Canadian Multiple Sclerosis Society and directed that this be placed before next year's meeting of General Council.

—Pursuant to correspondence from the Manitoba Division, directed the General Secretary to investigate the claims and advertising material disseminated in Canada by the Ball Clinic of Missouri and the Bragg Clinic of Florida and to determine whether action could be taken by the Postmaster General of Canada with regard to such advertising.

—Directed the General Secretary to attempt to locate a suitable delegate from the C.M.A. to the A.M.A. meeting in New York on June 25, 1961, in response to an invitation from the A.M.A. The name of Dr. N. Belliveau, Honorary Secretary of the Quebec Division, was suggested in this regard.

—Advised that the support of the Secretariat would be made available to the Saskatchewan Division in connection with their speeded-up schedule of hearings with the Saskatchewan Advisory Planning Committee on Medical Care, to the greatest possible extent, contingent upon demands related to activities of the Royal Commission on Health Care.

The next meeting of the Executive Committee will be held early in the autumn, on a date to be announced.

ACCIDENT AND SICKNESS INSURANCE CLAIM FORMS

At a recent meeting of the C.M.A.-C.H.I.A. Joint Committee on Uniform Claim Forms, it was reported that the uniform claim forms introduced by the C.M.A. and the Canadian Health Insurance Association have been very well received by the medical profession across Canada and also by the insurance industry.

Quite a few doctors sent in suggestions for changes. All of these have been very carefully considered by the Committee. It was their opinion that no major change should be made until the form had been in use for a trial period of one full year. However, in the meantime, they agreed to make the following changes immediately:

1. An Assignment, and a space to record the Policy Number and Employer, will be printed on the back of the form as follows:

"The following Assignment is printed at the request of The Canadian Medical Association.

ASSIGNMENT

(To be completed by the insured, if cheque is to be made payable to the Physician)

I hereby assign to .....
(Print name of Physician)

the medical and surgical benefits payable to me, but not to exceed the charge for the services described on this claim form. I under-

stand that I am financially responsible to the physician for charges not covered by this assignment and that it does not apply to comprehensive or major medical benefits.

Date ..... 19... Signed .....
Insured
Policy No. .....
Employer .....

2. In question 7(b) the word "total" will be inserted before "charge" so that the question will read "Your total charge". This is to provide greater clarity in the question.

3. To facilitate identification of a doctor as a specialist, the words "Certificated Specialist?" has been added on the line for the doctor's signature.

Most companies provide their policyholders with copies of the form, which are brought to the doctor for completion. One large company, and possibly a few very small companies, are relying on the doctors to use the pads of Combined Form CMHIA-1 supplied to them by the C.M.A. for their patients rather than having the company provide the forms. The advantages of this alternate method of distribution are to be evaluated at the end of the trial period. It is hoped, therefore, that physicians will co-operate in this experiment. It is understood that this company is distributing identification cards to their policyholders so that the policy number and name of the employer can be placed on the back of the form.

The C.M.A. representatives have pointed out that questions such as 11(a) and (b) on the Combined Form have a tendency to compromise the doctor, and place the onus on him to give answers which might more properly be answered by his patient. We are assured, however, that insurance companies require this information to determine eligibility for benefits, particularly for individual policies, and most companies find that the great majority of doctors are answering these questions satisfactorily. The fact that these questions are preceded by the words "to the best of your knowledge" would seem to adequately protect the doctor in answering these questions.

In a few instances, groups of doctors have modified the uniform Combined Form CMHIA-1 slightly for their own use. This of course defeats the whole purpose of having one approved uniform form, which was requested by the medical profession. All are therefore urged to co-operate with the insurance industry in their effort to encourage the use of only the approved uniform claim forms.

The Joint Committee of the C.M.A. and the Canadian Health Insurance Association is most grateful to the practising physicians in Canada for their co-operation in using the uniform forms, and for the constructive criticisms that have been sent to the C.M.A.

MEDICAL MEETINGS

MONTREAL PHYSIOLOGICAL SOCIETY

Under the auspices of the Faculty of Medicine of McGill University, Professor E. J. King, an ex-Canadian, now Professor of Chemical Pathology at the Postgraduate Medical School, London, spoke at the Royal Victoria Hospital on May 26 on "Enzymes in Clinical Diagnosis". Dean Lloyd Stevenson was chairman of the meeting. Professor King reviewed the earliest uses of enzyme tests for diagnosis. He pointed out that metabolic pathways depend on enzymes and if these enzymes are missing, metabolism is interrupted. Chemical reactions and the chemical substances taking part in reactions were discovered long before the catalytic agents in control of the reactions were elucidated. Thus the study of enzymes is comparatively recent. Sixty years ago measurement of diastase in the urine was carried out for the diagnosis of acute pancreatitis. This was the first time enzyme measurements were used for diagnosis. Nowadays serum amylase is estimated for the same purpose. Plasma lipase may be a more useful measurement because the rise following pancreatitis is more prolonged, but technically it is more difficult to measure. About 40 years ago investigations on alkaline phosphatases were instituted. Changes in its activity were seen in rachitic bone, rapidly growing bone, etc. Then, 25 years ago, acid phosphatases from the prostate were identified. It was observed that this enzyme was excreted in the urine of males, and that in cases of prostatic carcinoma with metastases to bone, much larger amounts of enzymes appeared in the urine. This is due to the fact that more is produced than is available from the prostate itself. After the discovery of stilbestrol by Dodds, and its application in therapy, it became possible to follow the effects of stilbestrol therapy by measuring acid phosphatase activity. The failure or success of therapy can be established biochemically before it shows up clinically. The acid phosphatases were the first enzymes that were shown to exist as a group of isoesterases. Twenty-five years ago only four or five enzymes had been studied. A major advance was made by Warberg when he elucidated the glycolytic enzymes in his studies of malignant tissue. In the late 1940's it was found that rats with tumours had high levels of phosphoglucomutase, isomerase and aldolase. Measurements of these enzymes have become extremely useful as adjuncts to the diagnosis of carcinoma of the breast. Aldolase levels are also changed in the presence of liver disease, muscular dystrophy and cardiac infarction. For the latter condition, a more useful test is the measurement of transaminase. In cardiac infarction there are large peaks of transaminase activity two to three days after the appearance of pain. Professor King stressed the value of serial estimations of transaminase to confirm the

Canad. M. A. J.
July 22, 1961, vol. 85

diagnosis and also to provide an estimation of the severity of the infarct. The lactic dehydrogenases are another group of isoesterases, and Professor King pointed out the confusion that surrounds this group owing to the existence of two systems of nomenclature, the U.S. system and the European system. By plasma electrophoresis on starch-gel a particular lactodehydrogenase and its tissue source can be identified. They can also be differentiated by heat inactivation. Phosphatases of bone, intestine and liver also have different features as isoesterases. For instance, they have different Michaelis constants. Professor King predicted future developments in "chasing enzymes [in blood] down and determining the tissues from which they arise." Today, enzyme measurements are useful in estimating the failure of therapy in treatment of carcinoma, and in predicting the extent of lesions in various diseases. In future, by making enzyme measurements it may be possible to diagnose disease before it becomes clinically manifest. First, the metabolic pathways will have to be elucidated, and then methods will have to be developed for studying the enzymes and the effects of disease on these enzymes. J. M. PARKER

GENERAL PRACTICE

1962 SCIENTIFIC ASSEMBLY CRUISE

COLLEGE members are assured of seeing lots of their colleagues at next year's scientific assembly aboard the *Empress of England*. More than 500 places have been booked by members and wives already, and the approximately 75-100 remaining cabins are now being offered to all Canadian physicians (and wives) on a first-come, first-served basis. Non-College members should address communications to the Executive Director of the College of General Practice.

An agent for the steamship company advises the College that both single and double cabins are still available.

The scientific assembly cruise ship sails from New York on March 26, for eight days, touching Bermuda and Nassau. Because the College has chartered all of the space on the 25,500-ton liner, rates are extremely low—ranging from about $200 and up per person. This price includes the cost of tours ashore at Bermuda and Nassau.

There will be daily scientific sessions led by eminent medical authorities, exhibits of interest to the medical profession and films on current medical subjects. Participation in the sessions, of course, permits the deduction of expenses so entailed, for income tax purposes if this is one of two conventions attended in 1962.

The total passenger list has been restricted to two-thirds of capacity so that all passengers aboard will have full run of a magnificent ship. There will be shipboard activities such as free dance instruction, deck tournaments, bridge and canasta parties, movies, floor shows and swimming in either the indoor or outdoor pools.

What to Wear

The first thing to remember when packing for your convention cruise is that the days are summer-like. The cruise divides itself into two phases—days at sea and days ashore. For days at sea, the sort of clothes suitable for the country club or beach will be just the thing for suntanning and swimming in the Lido deck pool. Such casual attire is appropriate for the enjoyable luncheon, served buffet-style on deck. In the dining room, however, jackets are always worn—shorts never.

For the man, business suits and ties are suggested at dinner time and the ladies will find that a summer cocktail dress will be quite the fashion.

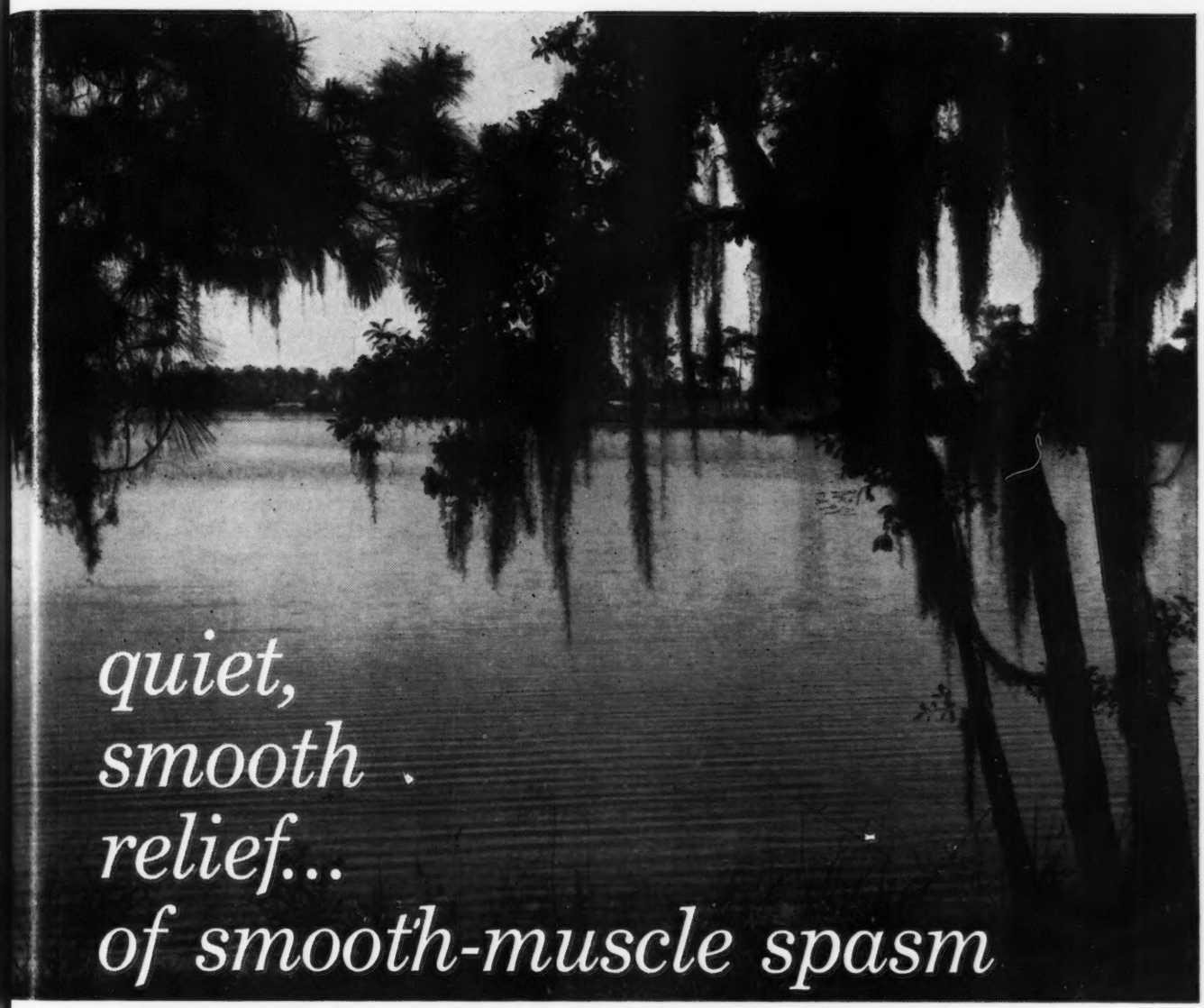
For going ashore, it is well to remember that citizens who spend their lives in the tropics dress for business with a view to comfort under the tropical sun—much as we dress for business in summertime in Canada. Ladies will find a couple of bathing suits, cottons, a cocktail dress and a smart casual cruise coat suitable for most occasions ashore. A scarf or turban will protect coiffures from tropic sun as well as being useful if churches are being visited.

Above all, remember to pack comfortable shoes for shore excursions.

Two things to keep in mind—a dinner jacket or dark business suit for the president's ball, for the men, and a simple evening or cocktail dress for the ladies; be sure to keep New York temperatures in mind and have clothes suitable for the start and finish of the cruise.

PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

Lister, like Hunter, never stood still; he was progressive. He had no sympathy with the man who saw finality in existing conditions. His attitude was much that of Hunter, of whom it is related that when Astley Cooper asked if he had not the year before stated an opinion on some point directly at variance with one he had just put forth, he replied, "Very likely I did; I hope I grow wiser every year." And to another of his pupils who asked him if he had not written so and so, "Never ask me what I have said, or what I have written; but if you ask me what my present opinions are I will tell you." Occasionally he would say to any of the pupils whom he saw taking notes, "You had better not write down that observation, for very likely I shall think differently next year."—A. Primrose: 1911 Address in Surgery to the Canadian Medical Association, *Canad. M. A. J.*, 1: 591, 1911.



PROBITAL

(BRAND OF PROPANTHELINE BROMIDE WITH PHENOBARBITAL)

rational ANTISPASMODIC formulation

PRO-BANTHINE® (7.5 MG.) AND PHENOBARBITAL (15 MG.)

PROBITAL combines two standard agents to assure easier management of patients with smooth-muscle spasm.

Acting together, Pro-Banthine and phenobarbital block excessive autonomic stimulation and screen disturbing external stimuli that often instigate and aggravate smooth-muscle spasm.

PROBITAL provides rational, convenient therapy in the less severe manifestations of spasm of small and large intestines, the pylorus, and the sphincter of Oddi, as well as in gastritis, biliary dyskinesia and diverticulitis.

PROBITAL is supplied as compression-coated tablets.

G. D. SEARLE & CO. OF CANADA LTD.
247 QUEEN ST., E., BRAMPTON, ONT.

Research in the Service of Medicine

Canad. M. A. J.
July 22, 1961, vol. 85

OBITUARIES

DR. JOHN W. A. ARMSTRONG, 91, anesthetist for several years at the Royal Victoria Hospital, Montreal, P.Q., died there on June 10. Dr. Armstrong graduated from McGill University Medical School in 1900 and practised in Dunham and Shawville prior to becoming resident anesthetist at the Royal Victoria Hospital. He retired from this position at the age of 65, but was recalled to the hospital during World War II. He continued to work there until his retirement 11 years ago.

He is survived by a son and daughter.

DR. JAMES A. COLVILLE, 89, died at St. Joseph's Hospital, Chatham, Ont., on May 22. Considered one of Kent County's oldest practising doctors until ill health forced him to retire last year, Dr. Colville had tended the sick at McKay's Corners for more than 50 years.

Born in Bowmanville, Ont., he graduated from the University of Toronto Medical School in 1899. After his internship in a London, England, hospital, he returned to Canada and opened his first practice in his hometown, Bowmanville. Because five other doctors were already practising there, Dr. Colville decided to move on to McKay's Corners, where he practised until his retirement.

He is survived by his widow.

DR. GEORGE H. EVOY, 57, died suddenly on May 31. Born in Rapid City, Man., he graduated from the University of Manitoba Medical School in 1929. During World War II he served for five years with the R.C.A.M.C. in Italy, France and Germany. Lately he was Senior Medical Officer of the Manning Depot. For the last two years he was physician at Deer Lodge Military Hospital.

Dr. Evoy is survived by his widow, a son and daughter.

DR. MATTHEW N. FARIS, 76, died in the Brantford General Hospital, Brantford, Ont., on June 6. A native of Bradford, Ont., he graduated from the University of Toronto Medical School in 1910 and interned at the Brantford General Hospital before opening a practice in Eagle Place where he practised for 50 years.

He is survived by his widow, a daughter and son, Dr. John W. Faris of Hamiliton, Ont.

DR. GORDON W. JONES, 41, died suddenly on June 4 at Brockville, Ont., where he practised for several years after graduating from the University of Toronto Medical School in 1945.

He is survived by his widow and daughter.

DR. EDWARD G. M. KENNEDY, 56, died in Belleville General Hospital, Ont., on June 5. A surgeon and physician in Belleville for 25 years, Dr. Kennedy had been a well-known football enthusiast during his school days. He represented Sarnia Collegiate Institute and Technical School, and the University of Western Ontario as a backfielder.

After graduation from the University of Western Ontario Medical School in 1932, he took over the practice of Dr. Bert Faulkner, a former Ontario Minister of Health. He retired from this practice last year.

He served overseas with the Royal Canadian Medical Corps during World War II and had been a past president of the Belleville Medical Association.

Surviving are his widow, a daughter and three sons.

DR. JOHN J. LEISHMAN, 53, died suddenly at his home in Fort Frances, Ont., on June 10. Born in Kenora, Ont., Dr. Leishman graduated from the University of Manitoba Medical School in 1934 and settled in Fort Frances four years later. He continued to practise there until his death.

He is survived by his widow and two sons.

DR. OLIVER J. A. LITTLE, 74, former head of the heart clinic at Sunnybrook Hospital, Toronto, Ont., died at his home on June 20. Dr. Little graduated from the University of Toronto Medical School in 1914, served overseas during World War I with the York Rangers, and returned to Toronto where he opened a practice.

Dr. Little is survived by his two sons.

DR. CHARLES LIGHTFOOT ROMAN, 72, died June 8 in the Montreal General Hospital, where he had been a consultant in industrial medicine for many years. A graduate of McGill University Medical School in 1919, Dr. Roman conducted a heart clinic at the Montreal General Hospital prior to his association with Montreal Cottons Ltd., Valleyfield, as a specialist in industrial medicine.

Considered one of the first physicians in Quebec to enter this field 40 years ago, Dr. Roman was made a Fellow of the Industrial Medical Association in 1953, and honoured at that organization's annual meeting in the same year. He retired in 1960 as chief medical officer for the Dominion Textile Company.

Dr. Roman is survived by his widow and five sons.

DR. CHARLES LIGHTFOOT ROMAN
AN APPRECIATION

With the death of Dr. Charles Lightfoot Roman the world has become a lonelier place. Dr. Roman was one of the kindest and friendliest men I have ever known. Even the most modest man takes some justifiable pride and joy in his own accomplishments, and no doubt this was true of Dr. Roman. Much more obvious and more strongly felt were the pride and joy he took in the accomplishments of his friends. Their good fortune, their achievements, their professional advancement, the honours they received—all were a source of happiness to him—and he promptly expressed his feelings in a beautifully worded letter written by hand or, in the last year when he was often too ill to write, by telephone. Always he was more interested in the welfare of others than of himself. Many great qualities contributed to his success in general practice and in the field of industrial medicine where he was a pioneer. When these qualities are recorded, love and devotion will lead all the rest. E.H.B.

BOOK REVIEWS

MEDICINE AS AN ART AND A SCIENCE. A. E. Clark-Kennedy and C. W. Bartley. 425 pp. J. B. Lippincott Company, Philadelphia and Montreal, 1960. $6.25.

This is not a textbook of medicine but rather a guide to a textbook, intended to cultivate a sense of perspective in the analysis of the patient's problems. The authors emphasize that diseases do not exist in splendid isolation as entities apart from the body which they happen to inhabit. Rather are they the resultant of interaction between the body and the pathogenic agent. A great variety of the reactions accounts for the great variety of disease patterns encountered. The study of the general principles of disease reactions on the part of the body, if applied intelligently to specific problems, undoubtedly reduces the amount of work necessary to memorize the facts about disease entities. Anyone experienced in undergraduate teaching realizes how difficult it is to get this viewpoint across to the student.

The discussion on organic disease is necessarily short and not intended to replace a standard textbook on medicine. It will therefore be of limited value except to the beginner. The part on functional disorders is all too brief to do justice to such an important topic. The section on clinical diagnosis will undoubtedly have the widest appeal. The principles of treatment are ably discussed. The text closes with some useful remarks about the ageing process, the very ill patient, and the dying patient.

Though this publication is directed primarily to the beginner, the reviewer believes that even the experienced clinician would benefit from reading much of the text.

FUNCTIONAL BEHAVIOR OF THE MICROCIRCULATION. A Monograph in The Bannerstone Division of American Lectures in Physiology. Benjamin W. Zweifach. 149 pp. Illust. Charles C Thomas, Springfield, Ill., 1961. $7.00.

The blood vessels of both man and animal have received considerable attention for many years because of their relationship to the ageing process and mortality statistics. The arteries, performing chiefly a transport function for the blood, have been the main subject of study, by both gross examination and conventional light microscopic methods. Of great interest today, largely because of newer and improved methods of study, is the vast capillary bed or microcirculation, that area of the vascular system where so many biological interactions and functions occur.

This monograph is written by an expert in the field who has contributed many papers on the subject over a period of many years. It can be divided into three almost equal parts, a description of the morphology of what comprises the microcirculation, a description of its function under what may be called physiological circumstances, and its behaviour in some pathological situations such as tissue injury and experimental shock. While the monograph is short, it is sometimes difficult to read, particularly in the earlier parts where there appears to be repetition. Some of the illustrations do not contribute greatly to the text, probably because they are from the less familiar field of direct or *in-situ* tissue microscopy. Electron microscopy is represented, but not as much as it might be.

The author points out that the monograph is intended as a frame of reference and an expression of a point of view rather than a source-book of information, a purpose which is achieved. Many reference works are cited, but not linked directly with the text. It is obvious that the surface has just been bared in the investigation of this dynamic part of the vascular tree, and this monograph is recommended to those who are interested in this field.

EVALUATION AND MANAGEMENT OF THE BRAIN-DAMAGED PATIENT. Jerome S. Tobis and Milton Lowenthal. 109 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1960. $6.50.

The aim of this volume is to encourage the development of a rational approach in the treatment of patients with damage to the brain. For this reason the authors have based their discussion on physiological principles and have emphasized the place of evaluation in establishing a program of treatment. They have drawn from their own extensive experience to amplify these points, and their conclusions are based on generally accepted sound principles of rehabilitation.

The subject is a large one and difficult to cover in a small space. A discussion of the nature of brain damage is followed by a brief account of the newer concepts of brain function and an analysis of various factors in brain damage. The importance of evaluation is emphasized. The second half of the book is devoted to the management of such patients, with a good description of the application of principles of rehabilitation to patients with four representative types of illness, the elderly hemiplegic, cerebral palsy, multiple sclerosis, and parkinsonism.

The result of compression of the material into this small space has been that the relationship between fundamental principles and detailed management is not always apparent, so that much of the purpose of the volume is lost. A less comprehensive account of management, more clearly related to established fundamental principles, would have been a help. Elaboration of language is sometimes responsible for lack of clarity. The illustrations are clear and helpful. There is a useful bibliography.

CONTROL OF MALNUTRITION IN MAN. Subcommittee on Control of Nutritional Diseases, American Public Health Association. 140 pp. American Public Health Association, New York, 1960. $1.50.

This 140-page paper-backed book contains about 35 concise, authoritative, up-to-date summaries, arranged under the headings of identification, etiology, occurrence, methods of control and treatment, of all the common types of malnutrition including obesity and anemia and some of the less common forms such as phenylketonuria and galactosemia. Twenty-five well-known authorities, including King, Mayer, Darrow, Stare, Vilter Woodruff, Brock, Moore, Andersen, Sebrell and Brett, have written the sections dealing with their own particular specialties. It is a very compact useful book.

Canad. M. A. J.
July 22, 1961, vol. 85

THE USE OF LSD IN PSYCHOTHERAPY: Transactions of a Conference on d-Lysergic Acid Diethylamide (LSD-25), April 22, 23 and 24, 1959. Edited by Harold A. Abramson, Biological Laboratory, Cold Spring Harbor, and State Hospital, Central Islip, New York. 304 pp. Illust. Josiah Macy, Jr. Foundation, New York, 1960.

This volume is a useful presentation of views and techniques in the use of the hallucinogen, lysergic acid diethylamide, either as a therapeutic agent or as an adjunct to psychotherapy.

There are 26 discussants, and a number of psychologists, ethnologists and biologists are included in the panel of authors. Five major topics are considered. Psychoanalytic therapy with LSD-25 is introduced by Abramson, who has a long experimental experience. The nature of the psychological response to LSD-25 is surveyed by the Jungian analyst and English mental hospital physician, R. A. Sandison. C. H. Van Rhijn presents an ingenious psychic model and describes a method of therapy called symbolysis. He utilizes a darkened room so that reality testing is "no problem" in spite of the very high doses of 400 gamma. He and a Canadian, Hoffer, describe the successful use of LSD in alcoholic cases.

The problems of LSD administration receive attention. Some five suicides have been recorded in LSD-25 subjects. In three of them, the relation to the drug is discounted. The importance of nursing and psychotherapy is stressed in avoiding these rare occurrences. Difficulty of communication in the course of LSD-25 is noted.

Of considerable use as a source book in ideas and approaches in hallucinogenic treatments of psychiatric disease, this volume gives the most lively and critical discussion of the field now available. The doctrinaire approach of some of the participants is tempered in discussion with colleagues of a different persuasion. The total effect of the book is, one feels, that the use of hallucinogenics in psychotherapy is still in a very early stage of development. The little that it has shown up to the present does, however, point in a number of stimulating research directions, viz. the exploration and evaluation of the individual therapeutic interview, the nature of hallucinations and symbolic thinking, neurobiochemical discovery, and the influence of social milieu on behaviour.

The book is highly recommended for those interested in the future of psychiatry.

FUNDAMENTAL NUTRITION IN HEALTH AND DISEASE. Mary C. Hiltz. 299 pp. Illust. The Macmillan Company of Canada Limited, Toronto, 1961. $3.75.

Approximately the first 100 pages of this book were published under the title "Nutrition" by the same author and publisher in 1955 and they have been slightly revised for inclusion in the present volume. This is an elementary textbook, apparently designed for pupil nurses or university students taking an introductory course in the subject. In some sections it is very simple; in a few it is too difficult for pupil nurses. A great deal of it is of purely academic interest and too little space is devoted to topics of practical importance. The sections on foods would be much more useful if more specific information was included. It does not contain enough accurate medical details to justify its use by pupil nurses. There are a great many very obvious typographical errors, as well as many misstatements and wrong interpretations of well-established medical and nutritional facts.

FRUSTRATION. The Study of Behavior Without a Goal. Norman R. F. Maier. 264 pp. Illust. Ambassador Books Limited, Toronto, 1961. $2.25.

This is the reissue, as a paperback, of a well-known psychological treatise published in 1949.

Beginning with an account of experimental data obtained from rats and verified in college students, the author presents the hypothesis that there are two types of behaviour, each of which follows different laws. First there is goal-directed behaviour which responds to reward and punishment, and second, when the impossibility of achieving a goal arises and frustration supervenes, "behaviour without a goal". This is marked by the appearance of aggression, fixation (or stereotypy) and regression to previous modes of successful behaviour; in short, a picture closely resembling certain neurotic and psychopathic behaviour in man. The way to deal with this type of behaviour is not by the traditional punishment, but by trying to reduce frustration, and by guidance thereafter.

The author then proceeds to apply his experimental findings to clinical psychology and psychiatry, showing how well they explain the known facts, and how they offer prospects for greater success in treatment and child-rearing.

This is an interesting book in that it shows that experimental backroom work can have eminently practical applications, provided that someone is prepared to straddle the enormous gap between the laboratory and the clinic. Few before or after Dr. Maier have tried. It is also interesting, since it challenges the basic assumption of psychoanalyst and experimental psychologist alike, who find themselves rather strange bedfellows in claiming that the symptoms of neurosis persist because they are rewarded, though the former talks of unconscious gratification and the latter of reinforcement.

Dr. Maier's conceptualization of frustrated behaviour, as an organism in decompensation, agrees well with the tenets of Jacksonian neurology, cybernetics and Pavlovian physiology but it must be considered still *sub judice*, and the book should be read in this light.

SURGERY OF THE ESOPHAGUS. Raymond W. Postlethwait and Will Camp Sealy. 482 pp. Illust. Charles C Thomas, Springfield, Ill., 1961. $30.00.

This is an excellent book which is based on experiences at the Duke Medical Center. In view of the fact that many aspects of disease of the esophagus are still new and some indeed are as yet unknown, this book serves as a good summary of present knowledge and with its excellent documentation of cases and complete bibliography as a stimulus to further work in this field.

This volume correlates well the new physiologic and anatomic discoveries with present-day diagnostic and therapeutic procedures.

The authors have inserted some very provocative discussion, and offer their own interpretation of many problems. They have proved in their writing their right to do so.

Chapters which are particularly good are those on congenital anomalies, hiatal hernia, reflux esophagitis and esophageal varices.

This book is comprehensive and very interesting. It is highly recommended.

MEDICAL NEWS *in Brief*

(Continued from page 208)

EMERGENCY HEALTH SERVICES ADVISORY COMMITTEE

The Honourable J. Waldo Monteith, Minister of National Health and Welfare, has organized, with Cabinet approval, an Emergency Health Services Advisory Committee, to assist and advise him in the execution of his civil defence powers, duties and functions in the health field.

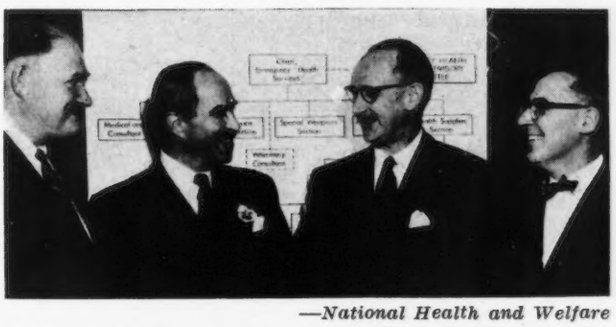
This committee will provide the necessary liaison with the medical and other health professions across Canada to ensure the co-ordination of planning for emergency health services and the efficient use of all available health workers in a national emergency.

Dr. G. D. W. Cameron, Deputy Minister of Health, has been appointed Chairman, with Dr. K. C. Charron, Director of Health Services, as alternate Chairman.

The Surgeon General, Canadian Forces Military Services, and the Director General, Treatment Services, have been appointed to the committee, together with representatives of national associations of the medical and allied health professions.

At the inaugural meeting held in Ottawa on May 29, the Canadian Medical Association was represented by Dr. A. F. W. Peart, Deputy General Secretary, who deputized for Dr. Harry Morton, the C.M.A. representative to the Advisory Committee.

(Continued on page 28)



—National Health and Welfare

Plans for health services and medical supplies under emergency conditions were studied at the first meeting of the recently established Emergency Health Services Advisory Committee. Pictured here (left to right) are: Dr. W. D. Piercey, Canadian Hospital Association, Toronto; Brigadier G. L. Morgan Smith, Deputy Surgeon-General, Canadian Forces Medical Services, Ottawa; Dr. G. D. W. Cameron, Deputy Minister of National Health, Department of National Health and Welfare and Dr. A. F. W. Peart, Canadian Medical Association, Toronto.

MEDICAL NEWS *in brief*

(Continued from page 27)

ACCIDENT FATALITIES IN CANADA

Accidents currently are responsible for the loss of more than 9000 lives a year in Canada. This is equivalent to a death rate of 54 per 100,000 population, or slightly higher than the rate of 52 per 100,000 recorded in the United States. Taking a relatively large toll at every period of life, accidents are by far the leading cause of death among children and young adults in Canada. Among males, they account for more than one-third of all deaths at ages 1-4, for over half those at ages 5-14, and for no less than two-thirds the total mortality at 15-24 years. Among females, accidental injuries cause about two-fifths of all deaths at ages 5-9, and at least one-fourth of the total at each of the other age groups under 25 years.

The accident death rate among males is 2⅝ times that among females at all ages combined, the rates in 1957-58 being 80.5 and 30.8 per 100,000, respectively. Males suffer the higher death toll at every age group, with the greatest difference occurring in early adult life. At ages 20-24, the accident death rates for the two sexes were 108.4 and 16.7 per 100,000, respectively, a ratio of about 6½ to 1; the disparity was almost as great at ages 25-44.

The motor vehicle accident death rate in Canada is 21 per 100,000 population, on a par with that in the United States. Two out of every 5 Canadian males killed in accidents sustain their injuries in motor vehicle mishaps; among females, the proportion is 1 in every 3. At no age group among males do motor vehicle accidents account for less than one-third of the total number fatally injured, and in the age range 15-24 years such accidents are responsible for somewhat more deaths than all other types combined. Among females at these ages, motor vehicle accidents account for about 70% of all fatal accidental injuries. In each sex, the large majority of the victims of motor vehicle accidents are occupants of cars—drivers and passengers. Pedestrian fatalities occur chiefly in childhood and at the older ages. There are also a goodly number of deaths annually among bicyclists — mostly boys 5-14 years of age—who sustain injuries in collisions with motor vehicles.

Falls rank second as a cause of fatal injury among both males and females at all ages combined, although the mortality from this cause is largely concentrated at the older ages. Three-fifths of the males and about nine-tenths of the females killed in falls are 65 years of age or older. In 1957-58, the death rate from falls at these ages was 76.8 per 100,000 for males and 102.2 for females; at the earlier ages, however, males recorded the higher rates. A recent study by the Dominion Bureau of Statistics showed that the majority of fatal falls occur in the home, and that many of them are among elderly people walking about the house; in such instances, physical weakness or impairment is often a contributing factor.

Drowning, accounting for more than 900 fatalities a year—exclusive of those associated with water transportation—recorded a death rate of 5.5 per 100,000 in 1957-58, nearly twice the rate in the United States. The death toll from accidental drown-

(Continued on page 30)

MEDICAL NEWS *in brief*

(Continued from page 28)

ing in Canada is about 5½ times as high among males as among females, the rates being 9.2 and 1.7 per 100,000, respectively, in 1957-58. Children and young adults are the main victims. The relative frequency of drownings among children 1-4 years of age is greater than at any other age except 15-24 years among males, and greater than at every other age without exception among females. Drownings associated with water transportation—the bulk of them involving small boats—add about 300 deaths annually; the majority of such fatalities occur among males in the age range 15-39.

Other types of accidents also contribute appreciably to the death toll in Canada. Fire and burns by other means rank fifth among males and third among females as a cause of accidental death; the mortality from such injuries is highest among young children and among older people, the groups least able to save themselves when a conflagration occurs. Accidents involving poisons (solids, liquids, or gases), firearms, and machinery are also among the leading types at various age groups.—*Statistical Bulletin* (vol. 42, April 1961), Metropolitan Life Insurance Co.

—

CANADIAN SOCIETY FOR THE STUDY OF FERTILITY

The eighth Annual Meeting of the Canadian Society for the Study of Fertility will take place at the Sheraton-Brock Hotel, Niagara Falls, Ontario, on October 27 and 28, 1961.

Further information may be obtained by writing to the Secretary, Dr. George H. Arronet, Infertility Centre, Royal Victoria Hospital, Montreal, Quebec.

—

DIFFICULTIES IN EVALUATING PUBLIC HEALTH PROGRAMS

In an article entitled "Evaluation as a Logical Process" (*Canad. J. Pub. Health*, 52: 185, 1961), A. C. Fleck, Jr. discusses some of the difficulties in evaluating public health programs. He points out that such evaluation threatens what is customarily done, since it always implies that there are alternative methods or goals which could be adopted. As a result, various defensive patterns are in use by those responsible for the programs; some are peculiar to governmental public health departments, while others are not.

Dr. Fleck, who is a physician and an evaluation consultant for the State of New York Department of Health, describes several varieties of difficulty for the evaluator. The following passage from his discussion illustrates one of the problems encountered.

"In our own and in other state organizations, the relevancy of any matter as a measure of effectiveness of the medical bureaucracy is determined by the medical judgment of the person least likely to view the operation without bias, the expert in charge of the program. Management and procedure analysts are always confronted with this fact. In one of our sister states, the Department of Finance attempted to evaluate the program of that state's Department of Public Health recently. In particular, the Department of Finance wished to find out something about the purposes and functions of this unit of government. They viewed the

definition of goals as a necessary prerequisite to evaluation. The inquirer wanted to know, 'What is the Health Department trying to accomplish?' The Department of Finance never found out and was apparently put off by the medical bureaucracy, the same way an individual physician might put off a patient's inquiry about his treatment. The printed report of this inquiry makes interesting reading. The management analysts tendered an apologia in the introduction by saying that the changing character of patterns of sickness and death made it impossible to develop an understanding of the purposes and functions of the department studied. Needless to say, the balance of the report tells us nothing about how well the programs were achieving their purpose. There could be no evaluation in this instance when there was acceptance of the medical expert's authoritative statement that things were so complex and dynamic that he could not say what he was trying to accomplish."

Further points of interest in the article are an emphasis on the essentially epidemiological character of public health programs, a description of the principles of evaluation, and a statement of the requirements for evaluation of a plan.

ACCIDENT STATISTICS

Accidents currently are responsible for the loss of more than 9000 lives a year in Canada, it is reported by statisticians of Metropolitan Life Insurance Company.

This is equivalent to an accident death rate of 54 per 100,000 population compared with the rate of 52 per 100,000 recorded in the United States. Taking a relatively large toll at every period of life, accidents are by far the leading cause of death among children and young adults in Canada.

The Canadian motor vehicle accident death rate, 21 per 100,000 population, is about the same as that of the United States. Two out of every five males killed in accidents sustain their injuries in motor vehicle mishaps; among females the proportion is one in three. Most of these fatalities occur among passengers or operators of automobiles. In addition, each year a number of young bicyclists are fatally injured in collisions with motor vehicles, the statisticians said.

Falls, largely concentrated in the older age groups, account for the second highest number of accidental deaths. A recent study by the Dominion Bureau of Statistics revealed that most fatal falls happen in the home, and that many of them occur among elderly persons simply walking about the house.

Drownings, apart from those in water transportation, take more than 900 lives a year in Canada, or 5.5 per 100,000 population. This is nearly twice the death rate in the United States.

Other important causes of accidental death in Canada include fire and burns, poisons, firearms, and accidents involving machinery.

M.N.I. FELLOWS' LECTURE

The Fifth Annual Fellows' Lecture, an annual lectureship established at the Montreal Neurological Institute and known as the Fellows' Society Annual Lecture, was delivered on June 7 by Dr. Guy L. Odom, Pro-

(Continued on page 32)

MEDICAL NEWS *in brief*

(Continued from page 31)

fessor of Neurosurgery, Duke University. He spoke on "Vascular Lesions of the Spinal Cord".

This lectureship is being endowed by contributions from Senior Fellows. The lecturers are chosen amongst the Senior (past) Fellows of the Institute and the lecture is delivered to present Fellows, visiting Senior Fellows, staff and guests. Past lecturers were Drs. Joseph Evans, Dorothy Russell, Webb Haymaker and Isadore Tarlov.

ASSOCIATION OF CANADIAN MEDICAL COLLEGES ESTABLISH SECRETARIAT

Thirty-five of every hundred doctors now commencing practice in Canada are graduates of foreign medical schools, according to Dr. G. H. Ettinger, Dean of the Medical College, Queen's University, and President of the Association of Canadian Medical Colleges.

Dr. Ettinger cited the shortage as one reason for the Association's decision, announced on June 15, to establish a secretariat in Ottawa for its twelve-member colleges. He announced that Dr. Wendell Macleod, Dean of the Medical College, University of Saskatchewan, will head the new secretariat as Executive Secretary of the Association. Dr. Macleod will take up his new appointment on January 1, 1962.

The secretariat will explore the problem of the decline in acceptable applicants for medical training and will work to devise ways and means to improve the situation. Steps will be taken to stimulate interest in medical careers among high school students.

"One problem may be the length of training and the cost of a medical education," Dr. Ettinger stated. "Through the secretariat, the Association will be able to study ways to improve this situation." At present, a medical education must involve six years of post-high-school training, plus a possible additional five years of specialist training.

Another problem to be tackled by the Association is that of obtaining in-hospital training for medical students.

"Medical education depends on the use of hospitals for clinical instruction," Dr. Ettinger explained. Formerly, such training had been carried out in public wards. The growth of hospital insurance had diminished this source. "We must now look for an agreeable formula by which instruction can continue in hospitals and this will be one task of the secretariat."

Curricula of medical schools will be studied with a view to standardizing training in all institutions.

Advice on the expansion of medical education facilities will be given by the secretariat to provincial Department of Education and Health. The secretariat will also work to establish accreditation of Canadian medical schools by Canadian standards. Hitherto, accreditation has been carried out by visiting teams of the Association of American Medical Colleges, the U.S. counterpart of the Canadian association.

It is expected that an unidentified U.S. foundation will assist financially in establishment of the secretariat.

Dr. Macleod was born in Kingsbury, Que., in 1905, and received his early education in Martintown and Winchester, Ont. He attended McGill University as a student in arts and medicine and did post-

(Continued on page 34)

INDEX TO ADVERTISERS

When writing to advertisers please mention the CANADIAN MEDICAL ASSOCIATION JOURNAL

NOTIFICATION OF CHANGE OF ADDRESS

(Please forward *one* month prior to effective date)

Name .....
(Please Print)

Former Address .....
(Please Print)

.....

Date effective .....

New Address .....
(Please Print)

.....

Please return to:

Canadian Medical Association,
150 St. George Street,
Toronto 5, Ontario.

MEDICAL NEWS *in brief*

(Continued from page 32)

graduate work at the Royal Victoria Hospital, Montreal, and Washington University, St. Louis, Missouri.

Dr. Macleod practised medicine in Montreal until 1941, at which time he entered the Royal Canadian Navy. He served as consultant in medicine and as Principal Medical Officer at H.M.C.S. *Stadacona*. During his service with the R.C.N., he was awarded the O.B.E. (Military Division). Dr. Macleod returned to civilian life in 1945 and resumed his practice in Montreal. Later, he practised medicine in Winnipeg and was lecturer in medicine at the University of Manitoba.

In 1951-52, he was awarded a Rockefeller Foundation fellowship to enable him to visit medical education centres in the U.S., the U.K. and Scandinavia, with a view to preparing him for his appointment as Dean of the College of Medicine, University of Saskatchewan. Dr. Macleod took up this position in 1952 and has occupied it since. During his tenure, the College expanded from a two-year to a full four-year medical course.

Dr. Macleod has been a member of the University of Saskatchewan Hospital Board and the Board of Directors of the Centre for Community Studies, Saskatoon. He served on the Canadian Forces Medical Council from 1958 to 1961 and for eight years has been on the Council of the Royal College of Physicians and Surgeons (Canada).

In 1957, he served as consultant to the Auckland (N.Z.) Medical Research Foundation and to the Auckland Regional Hospital Board.

In 1958, he was faculty member on a study tour and seminar in Yugoslavia, conducted under the auspices of the World University Service of Canada. He has served as consultant to hospitals in connection with postgraduate programs and was involved in the organization of the College of General Practice in Canada.

—

U.S. HOMICIDE STATISTICS

Homicide takes more than 8000 lives a year in the United States, according to the statisticians of the Metropolitan Life Insurance Company.

More than half of all the victims are slain by firearms, while in about one of four slayings, cutting and piercing instruments are employed.

The statisticians observe that the homicide rate among non-white males is over 10 times that among white males, the figures being 34.7 and 3.4 per 100,000, respectively, for 1958, the latest year for which complete data are available.

"The relative frequency of homicide is highest in the south, lowest in the north, while the west is in an intermediate position. In 1958, the rate ranged from 1.1 per 100,000 population in the New England States to 8.8 in the east south central area," the statisticians note.

Records for individual states are even more striking. Five states—New Hampshire, Rhode Island, Massachusetts, North Dakota, and South Dakota—recorded homicide rates of less than 1.0 per 100,000, New Hampshire having the lowest rate of 0.3. Three southern states, however, had rates exceeding 10.0 per 100,000: Alabama (11.4), Florida (10.7), and Georgia (10.4).